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THE NUMBER OF ISOTOPES AS A FUNCTION OF THE ATOMIC WEIGHTS OF THE ELEMENTS

E. P. Ozhigov

D.I. Mendeleev attached great importance to the ratios between the atomic weights of neighboring elements and element-analogs; in some regularities found by earlier and contemporary workers he saw the "seeds" of the periodic law [1].

Investigations aiming at an explanation of the ratios between atomic weights of neighboring elements were undertaken by several workers [2,3,4] and some of these studies [3,4] make a definite contribution to certain aspects of nuclear periodicity.

In the present paper an attempt is made to establish a functional dependence between the number of isotopes in the periods and the mean values of the differences of the atomic weights of the elements.

If such a dependence could be established, it would permit the prediction of the number of isotopes in a given part of the periodic system.

In view of the fact that a close genetic bond exists between neighboring and closely located elements of the periodic system, as evidenced by the isotopic composition of these elements [5], we have utilized in our calculations not the difference between neighboring elements but the averaged difference within the Mendeleev periods. The presence of nuclear periodicity of the Mendeleev type [2] is adequate theoretical justification for such a procedure.

In our calculations the limits of the periods were defined as the magnitudes obtained as the arithmetic mean between the atomic weights of the inert gases and the alkali metals. An exception is made for the end of the sixth and the start of the seventh periods where, due to the absence of element 87 in nature, the dividing boundary was assumed to be the atomic weight of radon.

The mean difference per element was obtained by dividing the length of the period in units of atomic weight by the number of elements. The neutron was assumed to be an element and was taken into account in calculating the mean atomic difference of the first period.

Analysis of the data brought to light an interesting dependence, involving the close similarity between the values of $\underline{R}^{\underline{r}}$ and the mean number of isotopes of the individual elements.

The calculations and literature data are presented in Table 1, from which we see that the number of isotopes in the periods known at the present time approximates the number found by the formula $\underline{N} \cdot \underline{R}^{\underline{r}}$ (where $\underline{N}$ is the number of elements in a period, $\underline{R}$ is the mean difference per element, and $\underline{r}$ is the exponent equal to $\underline{R}$.

The poorest agreement in the number of isotopes occurs in the sixth period. This might be due to the isotopic composition of all the elements of this period having still been studied inadequately. We may expect, in fact, the discovery of a considerable number of new isotopes in this part of the periodic system.

The physical significance of the expression $\underline{R}^{\underline{r}}$ may be revealed by analysis of the series of isotopes of individual periods. By an empirical method the author derived a rule which states that the number of isotopes in a period may be calculated from the formula $\underline{N} \cdot \underline{L}^{\underline{3}}$, where $\underline{N}$ is the number of elements and $\underline{L}$ is the mean tabular difference per element:

$$L = \frac{\text{series of isotopes of the period in mass numbers}}{\text{number of elements in the period}}$$

TABLE 1

Periods	Series of elements	Limits of periods (ends)	Length of period (in units of atomic wt.)	R	Numerical value of R^r	No. of isotopes in periods: Calcd. from formula $N \cdot R^r$	No. of isotopes in periods: found (Shpolsky [6])
1	H–He	5.47	5.47	1.82	2.97	6• + n = 7	6 + n = 7
2	Li–Ne	21.59	17.12	2.14	5.10	41	36
3	Na–Ar	39.60	19	2.37	7.73	62	45
4	K–Kr	84.59	46	2.55	10.88	196	173
5	Rb–Xe	132.10	48.51	2.69	14.32	256	217
6	Cs–Rn	222	90.90	2.84	19.38	620	296
7	Fr–U	238.53	17.53	2.50••	9.95	119••	80•••
				Total		1301	854

• Calculation performed for two elements, since the neutron does not form isotopes.

•• Since the isotopic composition of the elements of the end of the periodic system has not been completely established, the value of R is calculated from the first seven elements (including Np) and is extended over the whole 12 (including 97 and 98).

••• Isotopes of elements 97 and 98 are taken into account [7].

TABLE 2

Magnitudes compared	Periods 1	2	3	4	5	6	7
Atomic difference per element	2.00	2.25	2.55	3.30	3.50	2.90	2.2
"Isobaric number" per element	1.50	2.13	2.58	3.24	4.18	2.90	1.9

For example, the series of isotopes of the second period Li^6–Ne^{23} has a period length of 18. The mean difference per element in units of atomic weight is 2.25. The number of isotopes according to the formula $N \cdot L^2$ is 41, which is close to the number of isotopes found for this period (36). An explanation was later given of this empirical formula by comparing the magnitude of the mean tabular difference per element with our "isobaric number", which can be carried out fairly simply. For example, lithium has two stable isotopes, Li^6 and Li^7, the isotopes He^6 and Be^7 of shorter life periods will be related to the isotopes of lithium by the isobars:

$$\text{"Isobaric number" of lithium} = \frac{2+2}{2} = 2.$$

TABLE 3

Periods	Series of isotopes of the elements of a period	Number of isotopes: Predicted from formula $N \cdot L^2$ in 1946 [8]	Found in 1948 [9]	Calc'd from Petrovich's tables in 1948 [9]	Found in 1950 [6]
1	n(H)–He	8	6 + n	8	6 + n
2	Li–Ne	45	33	36	36
3	Na–Ar	50	44	54	45
4	K–Kr	140	157	200	173
5	Rb–Xe	167	206	227	217
6	Cs–Rn	276	246	270	296
7	Fr–U	44	40	84•	80
	Total	720	733	879	854

On summing the "isobaric numbers" of the stable isotopes of the elements of the second period and dividing the result by the number of these isotopes, we obtain a value of 2.125 for the "isobaric number" of the elements of the second period, which is close to the mean atomic difference per element for this period. "Isobaric numbers" for all the periods, taken from Petrovich's tables [9], are set out in Table 2.

• Calculated for the series Fr–U and extended over the 12 elements.

This table directly reflects the proportional dependence of the isobaric numbers on the number of isotopes entering into a series.

Hence we may assume that the magnitude L^2 or $L_1 \cdot L_2$ consists of the atomic difference per element and the "isobaric number" of both magnitudes calculated for the period.

By utilizing the formula $N \cdot L^2$ we succeeded in showing the trend and number of isotopes discovered in recent years.

Table 3 illustrates the good agreement of the number of calculated isotopes with the number subsequently found by experiment.

A defect of the formula $N \cdot L^2$ is that the number of isotopes calculated with its help is dependent on variables—the discovered isotopes of the alkali metals and of the inert gases.

Comparison of the number of isotopes found by the formulas $N \cdot L^2$ and $N \cdot R^r$ leads to the assumption that the expression $N \cdot R^r$ to a certain approximation expresses the limiting number of isotopes in the periods (without nuclear isomers).

This observation is also grounded in the fact that in the upper part of the periodic system the isotopic composition of many elements has remained nearly constant over a period of years; in the region of the pleiads, in fact, a regular transition is observed from the poorly stable β^+ active isotopes to the stable ones and then to the poorly stable β^- active isotopes.

Consequently, it appeared possible to derive a general formula for calculation of the number of possible isotopes in a given part of the periodic system.

This formula will have the following form:

$$S = 2R_1^r1 + 8(R_2^r2 + R_3^r3) + 18(R_4^r4 + R_5^r5) + 32R_6^r6 + N_7 \cdot R_7^r7,$$

where R is the mean atomic difference per element for the periods designated by exponents, r is the exponent equal to R, N is the number of elements in the seventh period, equal to 12 at the present time.

The physical significance of the expression R^r is the product of R and the possible "isobaric number" which approximates to R^r (Table 4)

TABLE 4

Periods	Mean no. of isotopes in the pleiad of the element	Isobaric No.	Calc'd no. of isotopes per element	
			Isobaric number · R	R^r
1	3	1.5	2.73	2.93
2	4.5	2.13	4.45	5.10
3	5.63	2.26	6.27	7.73
4	9.25	3.55	8.97	10.88
5	12.05	4.59	12.34	14.32
6	9.25	3.54	10.05	19.34
7	7.5	3.30	8.25	9.95

SUMMARY

1. It is established that the possible number of isotopes in the periods is a function of the magnitude of the mean atomic weights of the elements.

2. A formula is proposed for calculation of possible isotopes (excluding nuclear isomers) in a given portion of the periodic system which provides the possibility of prediction of the number of isotopes discovered in recent years, thus confirming the view of D.I. Mendeleev that the difference in atomic weights may be a "tool" for "more detailed check of the experimental data".

3. The idealistic and agnostic conclusion of bourgeois science about the unknowability of the possible number of isotopes and about the lack of correlation of the number of isotopes with the periodic system of D. I. Mendeleev [11] is refuted.

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FUSION DIAGRAMS OF THE TERNARY SYSTEMS: POTASSIUM SULFATE – CHROMATE – NITRATE AND SODIUM SULFATE – CHROMATE – NITRATE

I. S. Rassonskaya and A. G. Bergman

The ternary systems K_2SO_4, CrO_4, NO_3 and Na_2SO_4, CrO_4, NO_3 are part of the quaternary reciprocal system of the sulfates, chromates and nitrates of sodium and potassium which has been studied in the Fused Salts Laboratory of the N. S. Kurnakov Institute of General and Inorganic Chemistry of the Academy of Sciences of the U.S.S.R.

The binary systems formed by nitrates and the corresponding sulfates or chromates are characterized, according to various authors, by the presence of a simple eutectic and by the absence of compounds and solid solutions:

K_2SO_4–$(KNO_3)_2$ [1,2];	eutectic 333°; 97.5%	$(KNO_3)_2$,
K_2CrO_4–$(KNO_3)_2$ [3];	eutectic 336°; 96.5%	$(KNO_3)_2$,
Na_2SO_4–$(NaNO_3)_2$ [2,4];	eutectic 330°; 90.5%	$(NaNO_3)_2$,
Na_2CrO_4–$(NaNO_3)_2$ [3];	eutectic 300°; 91%	$(NaNO_3)_2$.

Our own data (Table 1) are in agreement with the literature data [3].

TABLE 1 Na_2CrO_4–$(NaNO_3)_2$

% Na_2CrO_4	t°	% Na_2CrO_4	t°	% Na_2CrO_4	t°
0	308	8	302	20	390
3	308	9	300	25	412
5	308	10	316	30	456
6	307	12	332	35	485
7	304	15	360	45	542

Hence in the investigated ternary systems the low-melting nitrates function as solvents, nonreactive with the solid phases formed from the sulfates and chromates. Due to the depression of the crystallization temperature, the presence of such a solvent may lead to the appearance on the liquidus diagram of the ternary systems of fields of crystallization of those phases which, in the absence of a solvent, in the binary systems are formed only as a result of solid-state transformations [2,3,5].

K_2SO_4–K_2CrO_4 [6]. The phase diagram is plotted from cooling and heating curves. A continuous series of solid solutions crystallizes from the liquid melts of potassium sulfate and chromate. Between the temperatures of 585 and 666°, corresponding respectively to the polymorphic transformation of pure K_2SO_4 and K_2CrO_4, the α-solid solutions of the hexagonal modification undergo transformation with formation of β-solid solutions of the rhombic modification.

Na_2SO_4–Na_2CrO_4 [7]. The phase diagram was studied with the help of cooling curves of melts of various compositions. A liquidus curve with a very weakly defined minimum indicates the existence of a continuous series of solid solutions.

A transformation curve is also found in the solid state, starting from 235° on the side of pure Na_2SO_4 and from 413° on the side of pure Na_2CrO_4.

In view of the fact that the sulfate and chromate exist above the specified temperatures in the form of hexagonal modifications isomorphous with each other, while below those temperatures they exist as isomorphous rhombic modifications, the author in question [7] concludes that there are two forms of solid solutions of the high-temperature hexagonal α-modification and of the low-temperature rhombic β-modification.

Since in the ternary systems under discussion the nitrate is a low-melting solvent which does not form either compounds or solid solutions with the sulfate and chromate, we can observe the fields of crystallization of both the α- and the β-solid solutions at the liquidus surface in the sodium system. The appearance of crystallization fields of the two types of solid solutions should only occur with the potassium system if it were possible to conduct the determinations at temperatures above 585°.

The fusibility was studied by the visual-polythermal method in glass test tubes. Supercooling of the melts was avoided by stirring with a platinum stirrer. The temperature of appearance of the first crystals was measured

TABLE 2

Sections of the ternary system K_2SO_4–K_2CrO_4–$(KNO_3)_2$

I		II		III		IV		V		VI	
8% K_2CrO_4 92% $(KNO_3)_2$ → K_2SO_4		10% K_2CrO 90% $(KNO_3)_2$ → K_2SO_4		15% K_2CrO_4 85% $(KNO_3)_2$ → K_2SO_4		20% K_2CrO_4 80% $(KNO_3)_2$ → K_2SO_4		$(KNO_3)_2$ → 30% K_2SO_4 70% K_2CrO_4		$(KNO_3)_2$ → 60% K_2SO_4 40% K_2CrO_4	
$\%K_2SO_4$	t°	$\%K_2SO_4$	t°	$\%K_2SO_4$	t°	$\%K_2SO_4$	t°	% melt	t°	% melt	t°
0	398	0	450	0	500	0	531	0	337	0	337
1	410	1	463	1	504	1	534	1	337	1	337
2	420	2	470	2	510	2	538	2	336	2	336
3	436	3	477	3	516	3	540	3	332	3	332
4	450	4	482	4	520	4	544	4	339	4	350
5	460	5	496	5	528	5	550	5	363	5	374
6	474	6	500	6	535	6	554	6	386	6	397
7	489	7	511	7	540	7	558	8	420	8	431
8	500	8	518	8	545	8	565	10	449	10	459
9	507	10	530	9	551			13	480	12	478
10	513							15	499	14	498
11	521							18	517	16	518
12	531							20	529		
13	541										

TABLE 3

Temperatures of Start of Crystallization of Melts in the Ternary System Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$ at the Sections

I		II		III		IV	
$(NaNO_3)_2$ → 75% Na_2SO_4 25% Na_2CrO_4		$(NaNO_3)_2$ → 50% Na_2SO_4 50% Na_2CrO_4		$(NaNO_3)_2$ → 25% Na_2SO_4 75% Na_2CrO_4		$(NaNO_3)_2$ → 15% Na_2SO_4 85% Na_2CrO_4	
% melt	t°	% melt	t°	% melt	t°	% melt	t°
0	308	0	308	0	308	0	308
2	308	3	308	4	305	3	305
4	308	6	308	6	303	6	304
6	308	8	304	8	301	9	300
8	304	10	303	10	300	12	312
10	302	12	300	13	313	15	333
12	298	15	298	15	324	18	354
15	324	18	330	18	344	20	370
18	358	20	345	22	379	23	388
20	390	23	374	25	404	26	408
22	400	25	387	28	417	29	426
25	422	30	433	30	435	33	452
30	460			35	464		
34.8	486						

with the help of a nichrome-constantan thermocouple of 0.3 mm cross-section and a 17 mV galvanometer. The error in the temperature determination was 1-2°. The thermocouple was protected against the action of the melt by a glass sheath. The weight of the sample was 2.5-3 g. Successive points on the section were obtained by the method of addition.

The starting preparations were obtained by recrystallization of chemically pure grades of materials; sodium chromate was prepared from sodium bichromate or chromic oxide and sodium carbonate followed by recrystallization.

I. System K_2SO_4–K_2CrO_4–$(KNO_3)_2$. 6 sections of this system were investigated (Table 2).

Fig. 1. Sections I to IV in the system K_2SO_4–K_2CrO_4–$(KNO_3)_2$.

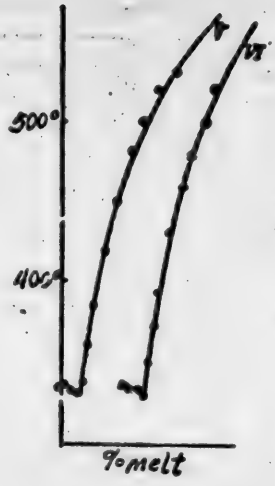

Fig. 2. Sections V and VI in the system K_2SO_4–K_2CrO_4–$(KNO_3)_2$.

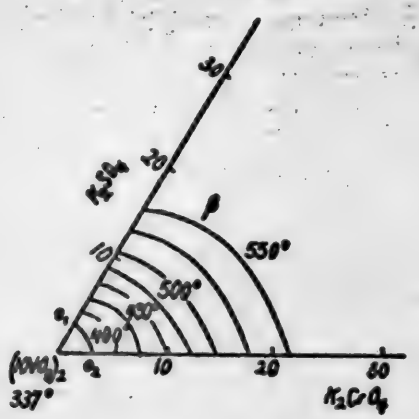

Fig. 3. Fusion diagram of the ternary system $K\|SO_4, CrO_4, NO_3$.

TABLE 3

V		VI		VII		VIII	
10% Na_2CrO_4 / 90% $(NaNO_3)_2$ → Na_2SO_4		12% Na_2CrO_4 / 88% $(NaNO_3)_2$ → Na_2SO_4		18% Na_2CrO_4 / 82% $(NaNO_3)_2$ → Na_2SO_4		21% Na_2CrO_4 / 79% $(NaNO_3)_2$ → Na_2SO_4	
% Na_2SO_4	t°	% Na_2SO_4	t°	% Na_2SO_4	t°	% Na_2SO_4	t°
0	306	0	323	0	366	0	391
1	306	1	323	1	366	1	391
3	307	2	323	2	366	2	391
5	307	3	323	3	366	3	391
6	307	4	323	4	366	4	396
7	316	5	323	5	371	5	400
8	327	6	323	6	376	6	405
9	333	7	330	7	380	7	410
10	344	8	340	8	386	8	416
11	360	10	360	9	393	9	423
13	380	13	388	11	405	11	435
15	400	15	406	13	418	13	445
18	429	18	429	14	425	14	450
20	446	20	445	16	441	17	468
23	470	23	470	18	457	18	480
28	505	26	491	20	487		

Corresponding to the first four sections is only one crystallization branch, relating to the separation of solid solutions of potassium sulfate and chromate (Fig. 1). On the radial sections issuing from the nitrate corner are two well-defined branches corresponding to the crystallization of nitrate and chromate-sulfate solid solutions (Fig. 2). The liquidus surface of the ternary system, represented in Fig. 3, consists of two fields corresponding to the crystallization of potassium nitrate and solid solutions of potassium sulfate and chromate.

The presence of potassium nitrate, which decomposes at 520-550° [8], prevented study of the fusibility at higher temperatures; consequently the solid solutions crystallizing in the investigated region consist of the β-modification which exists at below 585° [6]. The line of joint separation of potassium nitrate and the β-solid solutions has a minimum at 330° and the composition of 96% $(KNO_3)_2$ + 2% K_2SO_4 + 2% K_2CrO_4.

TABLE 3 (Continuation)

IX		X		XI		XII	
25% Na_2CrO_4 / 75% $(NaNO_3)_2$ → Na_2SO_4		29% Na_2CrO_4 / 71% $(NaNO_3)_2$ → Na_2SO_4		10% Na_2SO_4 / 90% $(NaNO_3)_2$ → Na_2CrO_4		13% Na_2SO_4 / 87% $(NaNO_3)_2$ → Na_2CrO_4	
% Na_2SO_4	t°	% Na_2SO_4	t°	% Na_2CrO_4	t°	% Na_2CrO_4	t°
0	412	0	442	0	304	0	350
1	414	1	445	2	309	2	354
2	416	2	447	4	314	4	358
3	420	3	449	6	323	6	365
4	424	4	451	8	332	8	371
5	428	5	453	11	350	10	377
6	431	6	457	13	365	12	386
7	436	8	462	15	378	14	398
9	447	10	467	18	394	16	411
11	454	13	478	20	407	18	421
13	464	15	484	22	422	20	435
15	478	18	498	24	435	22	446
20	495			27	448	24	457
				29	460	26	467

II. System Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$. 15 sections were investigated in the course of the study of this system. (Table 3).

On the first two sections (Figure 4) two branches are clearly visible, corresponding to the crystallization of $NaNO_3$ and of solid solutions of Na_2SO_4–Na_2CrO_4. Section III (Figure 5) has three branches, two of which, evidently belonging to the two types of solid solutions, intersect at a very obtuse angle. The crystals corresponding to these branches differ in outward appearance, which fact may serve as confirmation of the presence of different solid phases. Two branches appear on section IV (Figure 5); after the 8th point, however, the

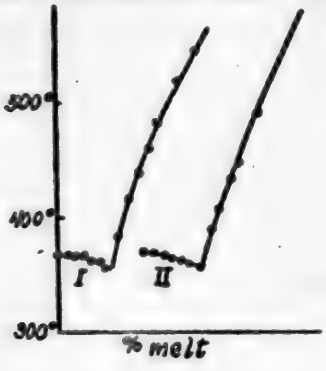

Figure 4 Sections I and II in the System Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$.

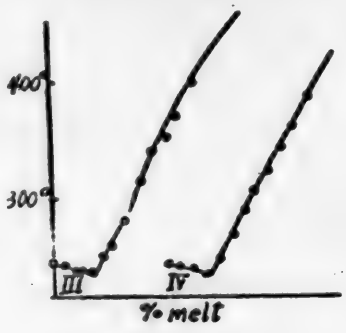

Figure 5. Sections III and IV in the system Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$.

outward appearance of the crystals changes appreciably and becomes the same as that of the crystals separating in sections I, II and III. Evidently, section IV, like section III, must consist not of two branches but of three. In sections V to VIII(Figure 6) there are two very well developed branches corresponding to crystals with differing forms – the two types of solid solutions. The second branches of sections V, VII, VIII (Figure 6), XI, XII and XIII (Figure 7) are initially slightly concave but subsequently become rectilinear. In the opinion of A. G. Bergman, sections V, VII and VIII consist of three branches, two of which form very obtuse intersection angles. Bergman therefore concludes that there is a field of crystallization of some other new solid phase. The sections from IX to XV are characterized by the presence of one regularly rising curve with a weak concavity corresponding to the crystallization of solid solutions of sodium sulfate and chromate.

No difference between the crystals of the solid phases separating throughout the whole extent of the section is detectable by the naked eye.

TABLE 3 (Continuation)

XIII		XIV		XV	
16% Na_2SO_4 / 84% $(NaNO_3)_2$ → Na_2CrO_4		19% Na_2SO_4 / 81% $(NaNO_3)_2$ → Na_2CrO_4		22% Na_2SO_4 / 78% $(NaNO_3)_2$ → Na_2CrO_4	
% Na_2CrO_4	t°	% Na_2CrO_4	t°	% Na_2CrO_4	t°
0	381	0	417	0	451
2	386	2	418	2	454
4	391	4	419	4	456
6	396	6	421	6	459
8	401	8	426	8	461
10	406	10	429	10	464
12	413	12	434	12	466
14	421	14	439	14	472
16	431	16	445	16	477
18	441	18	450	18	483
20	450	20	457	20	489
23	466	22	466	22	495
26	479	24	476		
29	498	26	486		

On the basis of the investigated sections, the fusion diagram of the ternary system Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$ was plotted (Figure 8). There is no doubt about the existence of three fields of crystallization: an extremely small field corresponding to the crystallization of sodium nitrate; a large field corresponding to the separation of α-solid solutions of sodium sulfate and chromate; and a small field adjacent to the Na_2CrO_4–$NaNO_3$ side corresponding apparently to the crystallization of the β-modification of the solid solutions of sodium sulfate and chromate. The broken curve marks the boundary of the internal field mentioned by A. G. Bergmann, corresponding to the crystallization of some new phase.

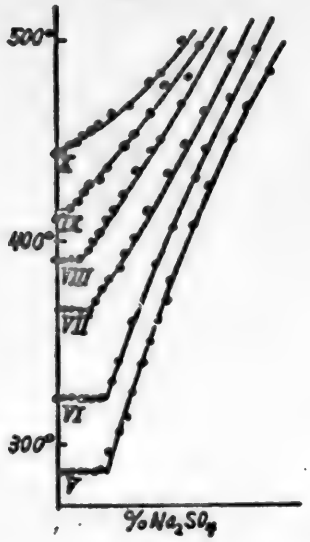

Figure 6. Sections V-X in the system Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$.

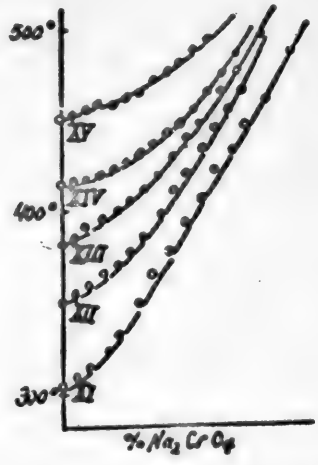

Figure 7. Sections XI-XV in the system Na_2SO_4–Na_2CrO_4–$(NaNO_3)_2$.

In order to determine the crystallization fields of the various solid phases, however, it is not always sufficient to study only the liquidus surface; in some cases it is necessary also to study the solid phases themselves. We attempted to clarify the problem to some extent by an investigation of these melts with the help of heating and cooling curves, using a differential recording device on N. S. Kurnakov's pyrometer. The temperatures of transformation of the pure salts that we found were: 241° for Na_2SO_4, 413° for Na_2CrO_4, and 276° for $NaNO_3$.

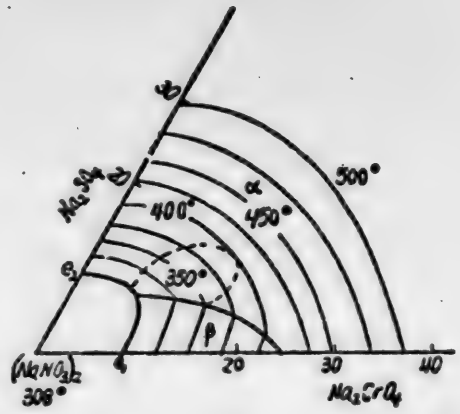

Figure 8. Fusion diagram of the ternary system Na ‖ SO_4, CrO_4, NO_3

Figure 9. Heating curve of the melt: 73% $(NaNO_3)_2$ + 17% Na_2SO_4 + 10% Na_2CrO_4

which were in good agreement with the literature values. The same may be said about the transformation temperatures in the solid solutions of the binary system of sodium sulfate and chromate. However, in repeated attempts to study the ternary melts by the method of heating and cooling curves. (Figure 9) we only detected the effects of transformation of sodium nitrate and of conjoint fusion of mixtures of nitrate with sulfate-chromate solid solution. The effect of transformation of the solid solutions of Na_2SO_4–Na_2CrO_4 evidently overlaps with that of the effects of transformation of sodium nitrate and of the joint fusion of sodium nitrate with the solid solution of Na_2SO_4–Na_2CrO_4. Due to the fact that the decomposability of sodium nitrate prevented investigation of melts other than those with a relatively low temperature of separation of the initial crystals, which are close to the nitrate corner [73-85% $(NaNO_3)_2$], it is understandable that the effects of transformation of nitrate and joint fusion of mixtures of nitrate with solid solutions of Na_2SO_4–Na_2CrO_4 must greatly predominate over all other effects, since there is a large proportion of nitrate in the melt but very little of the solid solutions separating in the form of initial crystals.

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THE DIAGONAL SECTIONS OF THE QUATERNARY RECIPROCAL SYSTEM OF THE FLUORIDES, CHLORIDES AND CHROMATES OF SODIUM AND POTASSIUM

N. S. Rassonskaya and A. G. Bergman

Further data on the quaternary reciprocal system Na, K‖F, Cl, CrO_4 are presented in this paper. Studies were previously made of the fusion diagrams of the ternary systems K‖F, Cl, CrO_4 and Na‖F, Cl, CrO_4 [1] on the basis of the prism shown in Figure 1. The ternary reciprocal system Na, K‖F, Cl has been investigated by Polyakov [2].

Double decompositions at the lateral faces of the prism of the reciprocal systems take place, according to the following equations, with the thermal effects indicated [3]:

$$K_2F_2 + Na_2CrO_4 \rightarrow Na_2F_2 + K_2CrO_4 + 8.24 \text{ kcal per equiv.}$$
$$269.02 \quad 319.8 \qquad 271.90 \quad 333.40$$

$$K_2Cl_2 + Na_2CrO_4 \rightarrow Na_2Cl_2 + K_2CrO_4 + 0.96 \text{ kcal per equiv.}$$
$$208.34 \quad 319.8 \qquad 196.66 \quad 333.40$$

$$KF + NaCl \rightarrow NaF + KCl + 7.28 \text{ kcal per equiv.}$$
$$134.51 \quad 98.33 \quad 135.95 \quad 104.17$$

The most stable diagonal is Na_2F_2–K_2CrO_4, whose thermal effect is equal to the sum of the thermal effects of the two other diagonals: 8.24 = 0.96 + 7.28.

Melts of the investigated quaternary reciprocal system possess, apart from general importance, practical interest as salt baths.

The salts utilized in the investigation were chemically pure grades which were recrystallized, then dried at 120° and calcined in a furnace at 500°. Temperatures of appearance and disappearance of crystals in melts of various compositions were determined visually in a platinum crucible, using a Pt-Rh–Au-Pt-Pd thermocouple with a diameter of 0.3 mm and a 17 mV galvanometer. The readings were accurate to 1-2°. Supercooling of the melts was prevented by using a platinum stirrer.

Section of Na_2F_2–K_2Cl_2–K_2CrO_4 (Figure 1). Two sides of this section are stable diagonals in the ternary reciprocal systems.

1. NaF–KCl, diagonal in the system Na, K‖F, Cl, possesses according to our data (Table 1) an inflection-eutectic point at 652° and 26.5% NaF.

2. Na_2F_2–K_2CrO_4, a diagonal in the system Na, K‖F, CrO_4, has an inflection point at 30% Na_2F_2 and 730°.

3. K_2Cl_2–K_2CrO_4 has been studied by S. F. Zhemchuzhny [4] and again by us.

The fusion diagram contains a eutectic point at 650° and 52% K_2Cl_2 and an inflection at 668° and 50% K_2Cl_2 at which intersection occurs of the crystallization branches of the two heteromorphic modifications of potassium chromate.

Fusibility in the diagonal section Na_2F_2–K_2Cl_2–K_2CrO_4 was studied along six cuts (Table 1, Figures 2 and 3).

The curves corresponding to the crystallization of NaF, K_2CrO_4 and KCl intersect at an acute angle. The branches corresponding to the separation of the α- and β-modifications of potassium chromate in some cases exhibit very slight breaks. Their detection and the establishment of the composition at the intersection points necessitated the determination of the temperature of separation of crystals from melts whose compositions differed by 1-2% of added salt.

TABLE 1

Cuts in the Diagonal Section of $Na_2F_2 - K_2Cl_2 - K_2CrO_4$ in the Quaternary Reciprocal System Na, K‖F, CrO_4 (in mole-%)

No.	Side NaF–KCl		Cut 1: 20% K_2CrO_4 + 80% K_2Cl_2 → Na_2F_2		Cut 2: 35% K_2CrO_4 + 65% K_2Cl_2 → Na_2F_2		Cut 3: 60% K_2CrO_4 + 40% K_2Cl_2 → Na_2F_2		Cut 4: 20% Na_2F_2 + 80% K_2Cl_2 → K_2CrO_4	
	%NaF	t°	%Na_2F_2	t°	%Na_2F_2	t°	%Na_2F_2	t°	%K_2CrO_4	t°
1	0	773	0	730	0	691	0	706	0	678
2	5	748	5	704	5	666	5	680	5	670
3	10	724	10	682	10	642	10	655	10	663
4	15	700	15	659	15	623	15	631	15	656
5	20	680	20	639	20	602	20	620	20	647
6	25	661	25	646	25	627	25	656	25	639
7	30	674	30	673	30	666	30	686	30	630
8	35	703	35	696	35	697	35	710	35	620
9	40	730	40	720	40	724	40	734	40	605
10	45	753	45	747	45	752	45	758	45	613
11	100	990	50	770	100	990	50	780	50	636
12			55	790			55	802	55	666
13			60	812			100	990	60	696
14			65	836					65	734
15			70	860					100	984
16			100	990						
17										

The constancy of the transformation temperature of the α- and β-modifications of K_2CrO_4 (666°) is evidence of the absence of solid solutions.

Consequently, judging by the character of the liquidus surface (Figure 4) the section $Na_2F_2 - K_2Cl_2 - K_2CrO_4$ must be classed as a stable section since the fusion diagram only contains fields of crystallization corresponding to the components forming this section: NaF, KCl and K_2CrO_4. The field of crystallization of potassium chromate on the 666° isotherm is divided into two surfaces corresponding to its two modifications.

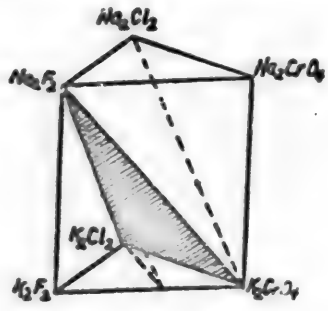

Figure 1. Distribution of sections in the prism of the quaternary reciprocal system Na, K‖F, Cl, CrO_4.

The fusion diagram of this stable diagonal section contains one ternary eutectic point and one inflection point.

The fields of KCl, NaF and β-K_2CrO_4 meet at the ternary eutectic; the latter corresponds to 44% K_2Cl_2 + 16% Na_2F_2 + 40% K_2CrO_4 and 580°.

The inflection point corresponds to 666° and the composition 16% K_2Cl_2 + 24% Na_2F_2 + 60% K_2CrO_4. This point is the juncture of the surfaces of crystallization of NaF, α-K_2CrO_4 and β-K_2CrO_4.

Section $Na_2F_2 - Na_2Cl_2 - K_2CrO_4$ (Figure 1). The sides of this section are: the binary system $Na_2F_2 - Na_2Cl_2$ and the diagonals $Na_2F_2 - K_2CrO_4$ and $Na_2Cl_2 - K_2CrO_4$ in the ternary reciprocal systems Na, K‖F, CrO_4 and Na, K‖Cl, CrO_4.

The fusion diagram of the system NaF–NaCl consists of two curves intersecting at the eutectic point corresponding to 674° and 33% NaF.

The polytherm of the system $Na_2Cl_2 - K_2CrO_4$ consists of five branches corresponding to the crystallization of α- and β-K_2CrO_4, chromglaserite ($3K_2CrO_4 \cdot Na_2CrO_4$), KCl and NaCl. The KCl crystallization branch is very short. The point of intersection with the diagonal of the line of joint crystallization of K_2CrO_4 and chromglaserite corresponds to 592° and 37.5% Na_2Cl_2.

The points of intersection with the diagonal of the lines of joint separation of chromglaserite with KCl and of KCl with NaCl correspond respectively to 540 and 536° and the compositions 47.5% Na_2Cl_2 and 53% Na_2Cl_2.

TABLE 1

Cuts in the Diagonal Section of Na_2F_2–K_2Cl_2–K_2CrO_4 in the Quaternary Reciprocal System Na, K F, CrO_4 (in mole-%)

Cut 5		Cut 6	
33% Na_2F_2 / 67% K_2Cl_2 → K_2CrO_4		25% Na_2F_2 / 75% K_2CrO_4 → K_2Cl_2	
$\%K_2CrO_4$	t°	$\%K_2Cl_2$	t°
40	603	0	770
42	602	10	722
44	602	20	679
46	605	22	673
48	612	24	665
50	628	26	659
52	636	28	654
53	642	30	647
54	649	33	636
55	656	36	624
57	666	39	613
60	687	42	600
65	720	45	598
100	984	48	609
		50	615
		55	634
		100	773

Fusibility in the diagonal section Na_2F_2 – Na_2Cl_2 – K_2CrO_4 was examined along with five cuts (Table 2. Figures 5 and 6).

The polytherms of the first four cuts have two branches, one of which corresponds to the crystallization of NaF. The second crystallizing phase (in the order of the cuts) will be: β-K_2CrO_4, chromglaserite, KCl and NaCl; the fifth cut, extending from the NaF-NaCl side to the K_2CrO_4 apex, has five branches corresponding to the crystallization of NaCl, KCl, chromglaserite, β-K_2CrO_4 and α-K_2CrO_4.

The crystallization surface obtained on the basis of the investigated cuts is represented in Figure 7. The greater part is occupied by the field corresponding to the separation of NaF.

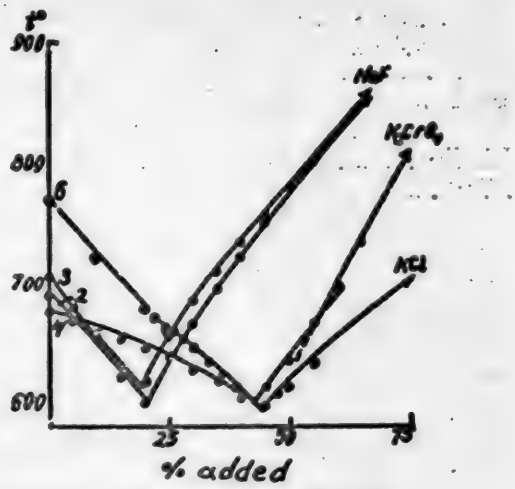

Figure 2. Cuts 2,3,4,6 in the diagonal section Na_2F_2 – K_2Cl_2 – K_2CrO_4.

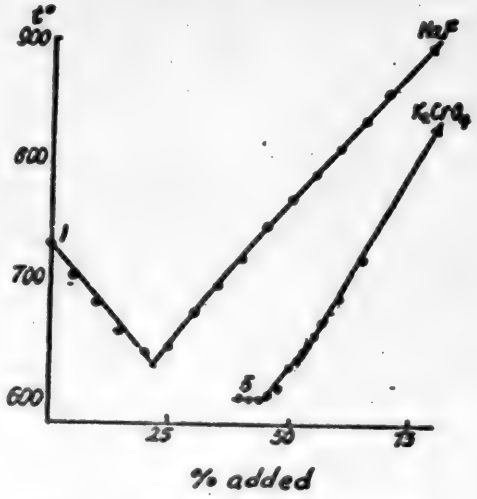

Figure 3. Cuts 1 and 5 in the diagonal section Na_2F_2 – K_2Cl_2 – K_2CrO_4.

The diagonal section Na_2F_2 – Na_2Cl_2 – K_2CrO_4 is unstable since the liquidus surface consists of six fields corresponding to crystallization of the three components of this section (NaF, NaCl and K_2CrO_4 in its two modifications) and the products of double decomposition (KCl and chromglaserite).

In the unstable section are the points A, B, C and D of common phase separation:

At point A, corresponding to 666° and 66% K_2CrO_4 + 20% Na_2F_2 + 14% Na_2Cl_2, simultaneous crystallization occurs of α-K_2CrO_4, β-K_2CrO_4 and NaF.

At point B, corresponding to 564° and 58% K_2CrO_4 + 5% Na_2F_2 + 37% Na_2Cl_2, crystallization takes place of NaF, β-K_2CrO_4 and chromglaserite.

At point C, corresponding to 526° and 47% K_2CrO_4 + 8% Na_2F_2 + 45% Na_2Cl_2, simultaneous separation of NaF, KCl and chromglaserite occurs.

At point D, corresponding to 528° and 45% K_2CrO_4 + 6% Na_2F_2 + 49% Na_2Cl_2, there is joint crystallization of NaF, NaCl and KCl. Low-melting melts of both of the sections: 1) 44% K_2Cl_2 + 16% Na_2F_2 + 40% K_2CrO_4

TABLE 2

Cuts in the Diagonal Section $Na_2F_2 - Na_2Cl_2 - K_2CrO_4$ of the Quaternary Reciprocal System Na, K ‖ F, Cl, CrO_4 (in mole-%)

Cut 1		Cut 2		Cut 3		Cut 4		Cut 5	
30% Na_2Cl_2 / 70% K_2CrO_4 → Na_2F_2		43% Na_2Cl_2 / 57% K_2CrO_4 → Na_2F_2		50% Na_2Cl_2 / 50% K_2CrO_4 → Na_2F_2		60% Na_2Cl_2 / 40% K_2CrO_4 → Na_2F_2		10% Na_2F_2 / 90% Na_2Cl_2 → K_2CrO_4	
% Na_2F_2	t°	% Na_2F_2	t°	% Na_2F_2	t°	% Na_2F_2	t°	% K_2CrO_4	t°
0	671	0	566	0	532	0	585	0	767
5	645	3	564	1	531	5	570	10	712
10	626	5	560	2	530	10	554	20	659
15	636	6	557	3	529	15	598	30	602
20	676	7	555	4	529	20	636	35	573
25	704	8	552	5	528	25	682	40	552
30	731	9	560	6	525	30	713	42	543
35	753	10	571	7	524	35	736	44	534
40	772	11	584	8	533	40	764	45	528
45	792	12	593	9	546	45	786	46	528
50	817	15	623	10	557	50	812	47	528
55	838	20	660	13	585	60	845	48	528
100	990	25	695	15	616	100	990	49	528
		30	723	20	658			50	538
		40	768	25	692			55	567
		100	990	30	722			60	586
				35	749			65	637
				45	804			70	680
				100	990			75	728
								100	984

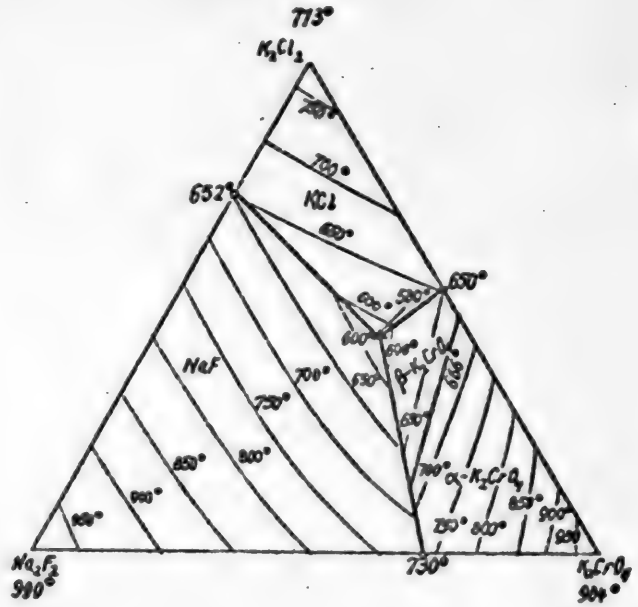

Figure 4 Liquidus surface of the diagonal section Na_2F_2–K_2Cl_2–K_2CrO_4

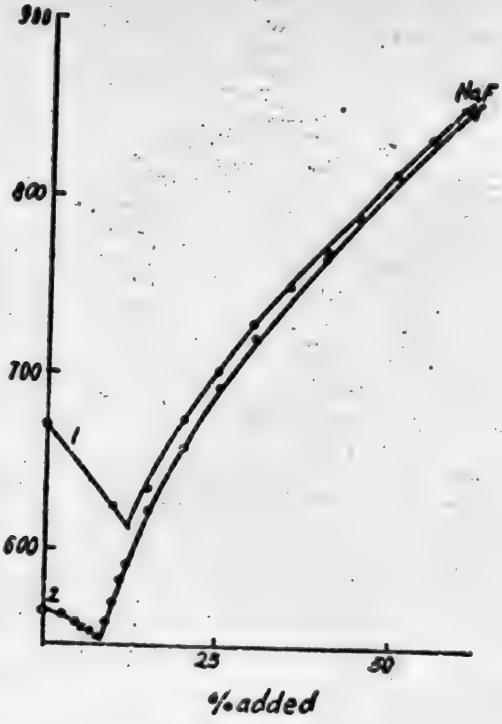

Figure 5 Cuts 1 and 2 in the diagonal section Na_2F_2–Na_2Cl_2–K_2CrO_4.

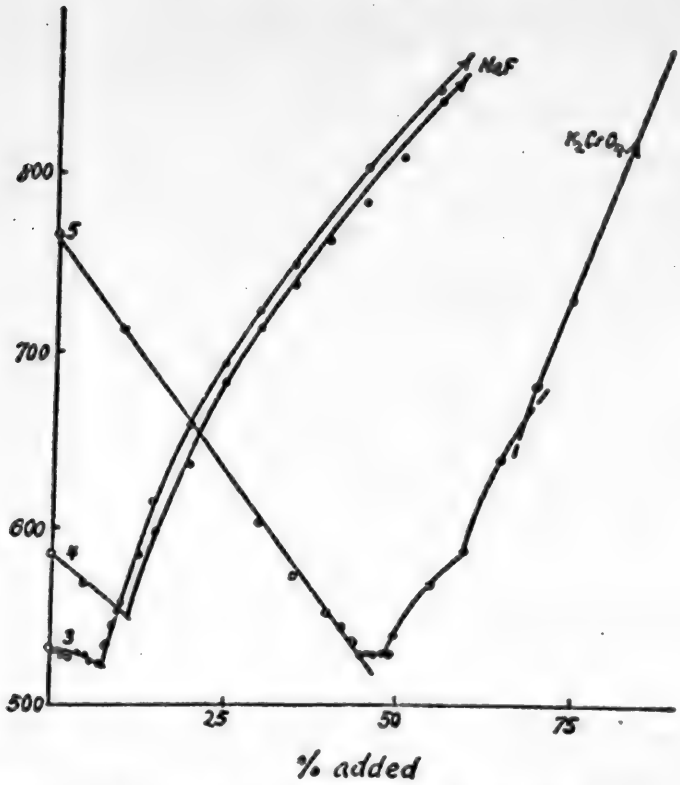

Figure 6. Cuts, 3, 4, 5 in the diagonal section $Na_2F_2 - Na_2Cl_2 - K_2CrO_4$

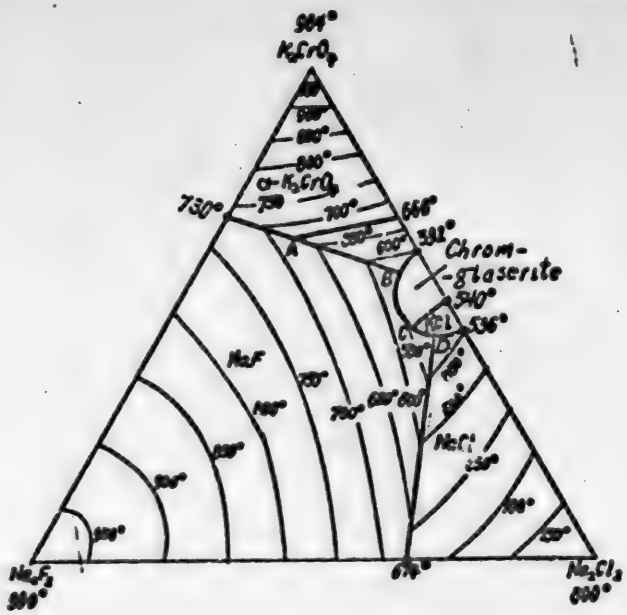

Figure 7 Liquidus surface of the diagonal section $Na_2F_2 - Na_2Cl_2 - K_2CrO_4$.

with melting point 580° and 2) 47% K_2CrO_4 + 8% Na_2F_2 + 45% Na_2Cl_2 (point C) with melting point 526° are of interest as salt baths.

The investigated quaternary reciprocal system is an analog of the system Na, K‖F, Cl, SO_4. Comparison of these systems permits clarification of the effect of replacement of the chromate ion by the sulfate ion on complex formation and on the shift of the double decomposition reactions.

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CLASSIFICATION OF THE RECIPROCAL SYSTEMS FORMED BY THE ALKALI METALS

G. G. Diogenov

About 200 reciprocal systems have been studied up to the present time. The investigation, as A. G. Bergman [1] has pointed out, has involved 25 cations and 30 anions. This is an enormous project, but it includes a relatively small proportion of the total number of metals (about one third) and by no means all the known anions. We are confronted with a great and intricate problem: To investigate nearly 50 cations and more than 10 anions. Particularly serious difficulties will be encountered and (we must hope) interesting results will be obtained in a study of the reciprocal systems involving cations of the eighth group, also cations of the rare-earth elements and of some subgroups of Mendeleev's periodic system.

We can justifiably say that the inclusion of these cations in the project will enrich chemistry not only by the discovery of new compounds but by the clarification of many problems relating to the nature of these cations and to their special position in the periodic system.

The wealth of material on the reciprocal systems obtained by the researches of a large group, centered mainly in the Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR (Moscow) but also operating in other towns (Rostov-on-Don, Voronezh, Irkutsk) enabled A. G. Bergman as far back as 1929 to set about classification of the data [2]; in this research A. G. Bergman and N. S. Dombrovskaya divided all the reciprocal systems into three types: reversible-reciprocal, irreversible-reciprocal, irreversible reciprical systems with a pronounced unilateral displacement of equilibrium (singular systems). This classification was correlated with the different thermal effects in double decompositions: For the first type the thermal effect is up to 2 kcal; for the second type it is 2 to 10 kcal; for the third type it is over 10 kcal.

The basis of this classification – the thermal effect of the reversible reaction – proved to be generally valid and has facilitated the correct characterization of the type of many reciprocal systems. But the accumulation of material on reciprocal systems with sharply defined complex formation and also with solid solutions and polymorphism compelled A. G. Bergman to greatly widen and supplement the original classification. In his latest publications [4] A. G. Bergman introduces new types of reciprocal systems: diagonal, adiagonal, mixed, rectangular and transition types, whose characteristics are correlated both with the thermal effect of the reversible reaction and with the triangulation of the reciprocal systems.

Experiment shows that even this broadening of classification does not embrace all types of ternary reciprocal systems, and it is not in our opinion definitive. We must conclude that a broader classification of reciprocal systems will be created only by taking into account the position of the cations in Mendeleev's periodic system, i.e., we should start on the basis of a natural law which knows no exceptions and is the preeminent instrument for gaining insight into the nature of matter.

In the study of the alkali nitrate and alkali chromate reciprocal systems with participation of cations of the main subgroup of the first group of the periodic system, the thermal effect of these reactions, arranged in a definite order, engaged our attention owing to its periodicity. Further investigations showed that all other reciprocal systems formed by alkali cations also exhibited periodicity in their thermal effects. This observation prompted us to take this characteristic as a basis of classification of reciprocal systems formed with alkali metals.

Our approach will be clarified by a few examples (see table).

In this table are included 10 possible reciprocal systems for four pairs of anions ($OH'-NO_3'$, $OH'-Cl'$, $OH'-CO_3''$, $F'-Cl'$).

The principle of arrangement of the reciprocal systems according to groups has the following basis. In the first group are included all those reciprocal systems which are formed by adjacent alkali metals. As we see from the table, the thermal effect of these reactions decreases in a regular manner. In the second group of reciprocal systems are included those systems which are formed by alkali metals separated by one other element in the periodic system. The thermal effect of these systems also regularly declines from top to bottom. In the third group of reciprocal systems are brought those systems containing alkali metals separated from one another in

the periodic table by two elements. Their thermal effect (in passage from top to bottom) also regularly falls. The fourth group contains the first alkali metal (lithium) and the last one in the periodic table (cesium). Here the thermal effect is at a maximum.

The fall in thermal effect is a feature of all the groups. The first systems in the groups exhibit the most pronounced displacement of equilibrium; this gradually diminishes and reaches its lowest value in the bottom of the groups.

On comparing the horizontal series of the table, we see that the thermal effect of the respective reciprocal systems continuously increases from the first group to the last. At the start of the series are reciprocal systems with the smallest displacement of equilibrium and there is a gradual increase to a maximum in the last series.

TABLE

	Reciprocal systems							
	1st group		2nd group		3rd group		4th group	
series	system	thermal effect (in kcal)	system	thermal effect (in kcal)	system	thermal effect (in kcal)	system	thermal effect (in kcal)
1	Li, Na ‖ OH, NO_3	11.2	Li, K ‖ OH, NO_3	17.3	Li, Rb ‖ OH, NO_3	19.1	Li, Cs ‖ OH, NO_3	22.0
2	Na, K ‖ OH, NO_3	6.1	Na, Rb ‖ OH, NO_3	7.9	Na, Cs ‖ OH, NO_3	10.8	–	–
3	K, Rb ‖ OH, NO_3	2.0	K, Cs ‖ OH, NO_3	4.7	–	–	–	–
4	Rb, Cs ‖ OH, NO_3	3.0	–	–	–	–	–	–
1	Li, Na ‖ OH, Cl	15.4	Li, K ‖ OH, Cl	21.0	Li, Rb ‖ OH, Cl	22.7	Li, Cs ‖ OH, Cl	25.1
2	Na, K ‖ OH, Cl	5.7	Na, Rb ‖ OH, Cl	7.3	Na, Cs ‖ OH, Cl	9.7	–	–
3	K, Rb ‖ OH, Cl	1.6	K, Cs ‖ OH, Cl	4.0	–	–	–	–
4	Rb, Cs ‖ OH, Cl	2.4	–	–	–	–	–	–
1	Li, Na ‖ OH, CO_3	4.3	Li, K ‖ OH, CO_3	6.4	Li, Rb ‖ OH, CO_3	6.8	Li, Cs ‖ OH, CO_3	7.1
2	Na, K ‖ OH, CO_3	2.1	Na, Rb ‖ OH, CO_3	2.5	Na, Cs ‖ OH, CO_3	2.8	–	–
3	K, Rb ‖ OH, CO_3	0.4	K, Cs ‖ OH, CO_3	0.7	–	–	–	–
4	Rb, Cs ‖ OH, CO_3	0.3	–	–	–	–	–	–
1	Li, Na ‖ F, Cl	10.2	Li, K ‖ F, Cl	18.4	Li, Rb ‖ F, Cl	19.9	Li, Cs ‖ F, Cl	22.6
2	Na, K ‖ F, Cl	8.2	Na, Rb ‖ F, Cl	9.7	Na, Cs ‖ F, Cl	12.4	–	–
3	K, Rb ‖ F, Cl	1.5	K, Cs ‖ F, Cl	4.2	–	–	–	–
4	Rb, Cs ‖ F, Cl	2.7	–	–	–	–	–	–

Consequently, in passing from one group of reciprocal systems to another we observe that the thermal effect regularly falls in the first group, then sharply rises in the second group, then gradually falls, and once again sharply rises at the start of the third group, and finally again falls and sharply rises in the fourth group.

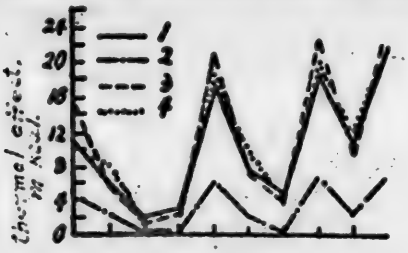
Thus the thermal effect of reciprocal systems formed by the alkali metals changes periodically within the framework of the Mendeleev periodic group, as is clearly illustrated in Figure 1.

The foregoing considerations permit a new approach to the problem of classification of reciprocal systems. The reciprocal systems possible for the alkali metals are divided into ten types, the type of the system being determined by its place in the table. For example, a system formed from lithium and sodium, independently of the anions, will always be located in the first group and first series and is, as a rule, an irreversible system. Systems formed from sodium and rubidium must go into the second group and second series of reciprocal systems. Systems of this type will most usually be irreversible-reciprocal and their equilibrium shift (for a given pair of anions) will be greater than in systems belonging to the first group and second series of reciprocal systems.

The chief advantage of this classification is that it is closely linked to the periodic system of the elements and supplies an unequivocal answer to the question: What is the character of a given system and how is it related to reciprocal systems of other pairs of alkali metals (for a given pair of anions)?

Utilization of the proposed classification enables the effect of anions on the equilibrium shift in reciprocal systems to be more easily explained. It is clear from the table, in fact, that reciprocal systems of one

type (systems occupying one and the same position in the classification table) with identical cations and a common ion (in our case hydroxyl) have a considerably greater shift of equilibrium in the case of the Cl^- ion (radius 1.81 A), a rather smaller shift if the second anion is NO_3^- (radius 2.36A), and a quite insignificant equilibrium shift when the CO_3^{--} ion (radius 2.57A) is present. This regular change in equilibrium shift in the systems appears to us to be in direct correlation with the magnitude of the ionic radius. The equilibrium shift is greater in systems (other conditions being equal) in which the anion has a smaller radius.



Change of thermal effect of double decomposition in reciprocal systems formed by the alkali metals.

Systems: 1) alkali nitrate, 2) alkali carbonate, 30alkali chloride, 4) chloride fluoride.

The proposed classification is valid in our opinion for reciprocal systems formed by metals of one group and does not embrace reciprocal systems formed by metals of different groups of the periodic system. But this fact by no means implies the incorrectness of our considerations; rather does it show that we have succeeded in dealing with only part of the complex and interesting problem. Other research work, possibly on a larger scale, on the classification of reciprocal systems awaits fresh investigators and the accumulation of supplementary experimental material.

SUMMARY

1. The thermal effect of reciprocal systems formed by the alkali metals varies periodically within the limits of the groups of the Mendeleev system.

2. The reciprocal systems possible for alkali metals are classified into ten types, the type of system being determined by its position in a table compiled on the basis of the distance between the alkali metals in the periodic system.

3. Equilibrium in the reciprocal systems is displaced the more strongly the smaller the radius of the anion (with an identical pair of cations and a common anion – in our case hydroxyl).

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CHARACTERISTIC PROPERTIES OF ALKALI HYDROXIDE-NITRATE SYSTEMS

G. G. Diogenov

The systematic study of reciprocal systems of one exchange decomposition enables the observation of certain regularities characterizing the given reciprocal systems and underlining their difference from systems of another exchange decomposition. In particular, systematic studies permit the establishment of preliminary statements about the specific properties of the anions undergoing transformations in the systems. For example, it is very probably correct to say that the OH^- ion always increases the numer of compounds in systems, while the NO_3^- ion very often leads to stratification. The F^-, Cl^- Br^- and I^- ions generally form systems with a small number of compounds and the thermal effect of these reactions (for a given pair of cations) changes periodically within a given group of the periodic system of Mendeleev. More singular systems are formed by nonmetals separated in Mendeleev's periodic system by one or two elements; systems with a smaller equilibrium shift are always formed by nonmetals arranged in Mendeleev's table side by side. The foregoing observations are well illustrated by Table 1 and Figure 1.

TABLE 1

Exchange decomposition	Series	First group		Second group		Third group	
		Reciprocal systems					
		Systems	Thermal effect	Systems	Thermal effect	Systems	Thermal effect
Lithium-sodium	1	Li, Na ‖ F, Cl	10.2	Li, Na ‖ F, Br	12.59	Li, Na ‖ F, I	13.82
	2	Li, Na ‖ Cl, Br	2.29	Li, Na ‖ Cl, I	3.52		
	3	Li, Na ‖ Br, I	1.23				
Lithium-cesium	1	Li, Cs ‖ F, Cl	22.6	Li, Cs ‖ F, Br	27.78	Li, Cs ‖ F, I	32.71
	2	Li, Cs ‖ Cl, Br	5.22	Li, Cs ‖ Cl, I	10.15		
	3	Li, Cs ‖ Br, I	4.93				

Similar regularities are exhibited in other halide exchanges; but although halide exchange is interesting in many respects, it is not the main subject of our discussion. In the present paper we wish to consider rather more closely the alkali hydroxide-nitrate exchange decomposition which attracts our interest both from the theoretical aspect (ortho salts, stratification, periodicity) and from the practical aspect since many melts of the reciprocal systems of this exchange can be recommended as heat transfer media.

We present the most important properties of the reciprocal systems of alkali hydroxides and nitrates in a table and we then discuss the data. The 10 possible systems of alkali hydroxides and nitrates are listed in Table 2. In the first group of this table are arranged the reciprocal systems formed by alkali metals occurring side by side in Mendeleev's periodic system. Their thermal effect (within the group), and consequently also the degree of shift of equilibrium, decreases in passage from top to bottom. The second group contains reciprocal systems formed by alkali metals which are separated from one another by one element in the periodic system. Their thermal effect, and consequently the degree of shift of equilibrium, (within the group), likewise decreases as we pass from top to bottom.

In the third group are reciprocal systems formed by alkali metals separated from one another in the periodic system by two elements. The thermal effect of these reversible reactions and the equilibrium shift (from top to bottom) also regularly decrease. The fourth group contains the reciprocal system formed by the first metal in the series (lithium) and the last metal (cesium). Its thermal effect and the degree of equilibrium shift are at a maximum. We thus see that the thermal effect of reciprocal systems formed by the alkali metals changes periodically within the first group of the Mendeleev system.

Stable pairs in all the reciprocal systems are formed by the alkalis with lower molecular weight and nitrates with higher molecular weight (and, as a rule, with higher melting point, except in the system K, Rb ‖ OH, NO_3,

TABLE 2

Groups	Series	Systems	Thermal effect (in kcal)	Stable pair	Stratification	Notes
I	1	Li, Na‖OH, NO_3	11.2	LiOH–$NaNO_3$	No	System studied by G. G. Diogenov
	2	Na, K‖OH, NO_3	6.1	NaOH–KNO_3	No	System studied by N. A. Reshetnikov
	3	K, Rb‖OH, NO_3	2.0	KOH–$RbNO_3$	No	Not investigated
	4	Rb, Cs‖OH, NO_3	3.0	RbOH–$CsNO_3$	No	Not investigated
II	1	Li, K‖OH, NO_3	17.3	LiOH–KNO_3	Yes	System studied by G. G. Diogenov
	2	Na, Rb‖OH, NO_3	7.9	NaOH–$RbNO_3$	Yes	Stable diagonal investigated by G.G.Diogenov (Figure 2)
	3	K, Cs‖OH, NO_3	4.7	KOH–$CsNO_3$	Yes	Not investigated
III	1	Li, Rb‖OH, NO_3	19.1	LiOH–$RbNO_3$	Yes	Stable diagonal investigated by G.G. Diogenov (Figure 2)
	2	Na, Cs‖OH, NO_3	10.8	NaOH–$CsNO_3$	Yes	Not investigated
IV	1	Li, Cs‖OH, NO_3	22.0	LiOH–$CsNO_3$	Yes	Not investigated

which for that reason also deviates from the general regularity in change of thermal effect in the first group).

The alkali hydroxide-nitrate exchange decomposition is characterized by the occurrence of stratification in the six reciprocal systems (Figure 2). It is interesting that stratification is observed in the second, third and fourth groups, i.e., in those reciprocal systems formed by alkali metals between which one other metal is located in the periodic system (second group) between which are two other metals (third group), or between which are three

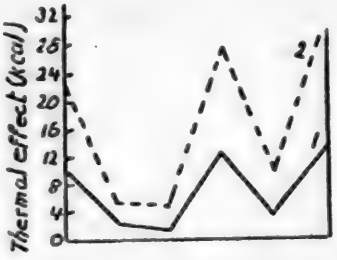

Figure 1. Halide exchange decomposition. 1) Lithium-sodium exchange decomposition; 2) lithium cesium exchange decomposition.

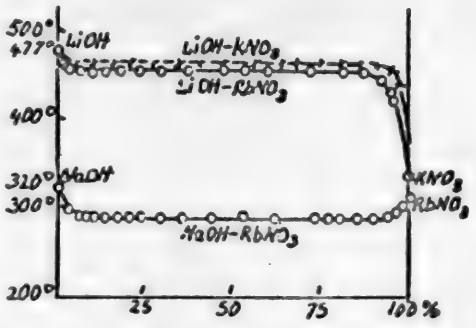

Figure 2: Alkali hydroxide-nitrate exchange decomposition with stratification.

other metals (fourth group). No stratification is observed in the first group of reciprocal systems. It is seen from Table 2 that we were unable to confirm all our conclusions experimentally (due to the absence of cesium compounds), but we are fully convinced of the validity of our conclusions regarding the systems Na, Cs‖OH, NO_3 and Li, Cs‖OH, NO_3, because they exhibit a more pronounced equilibrium shift than systems preceding them and the occurrence of stratification in them has been experimentally demonstrated. In our opinion, stratification must also occur in the system K, Cs‖OH, NO_3, since it belongs to the second group, a characteristic of which is stratification. It is usually considered that stratification is observed in reciprocal systems with a large thermal effect (20 kcal and more). We consider that the magnitude of the thermal effect is by no means a criterion for anticipating stratification in reciprocal systems. Indeed in the alkali hydroxide-nitrate exchange decomposition, the system Li, Na‖OH, NO_3 has a thermal effect of 11.2 kcal and yet no stratification is observed in it, whereas the systems Na, Rb‖OH, NO_3 (thermal effect 7.9 kcal) and Na, Cs‖OH, NO_3 (thermal effect 10.8 kcal) are characterized by stratification.

If stratification is possible in a particular exchange decomposition (we are speaking of systems formed by metals of one group of the periodic system), then it will always be observed in those reciprocal systems which

are formed by metals separated from each other in the periodic system by one, two or three elements. In the last case stratification will be at a maximum.

Experiments show that stratification is governed not only by the cations but also by the nature of the anions. Stratification is observed most frequently of all in reciprocal systems containing the NO_3' anion. For example, stratification is observed all along the stable diagonals of $TeNO_3$-AgCl, KNO_3-TlBr, KNO_3-TeI, as well as in the binary systems $NaNO_3$-AgCl, $NaNO_3$-AgBr, KNO_3-AgCl, KNO_3-AgBr. It is difficult to account for the special tendency of nitrates to form strata, but it is very probably associated with the low melting point of these compounds and the marked difference between their structure and that of the other component of the pair. We can expect this problem to be likewise clarified by further investigation of the reciprocal systems in other groups of the periodic system of the elements.

The following features are also very characteristic of alkali hydroxide-nitrate interchange: 1) occurrence of solid solutions on the sides formed by alkalis; 2) a fairly large number of compounds in the systems; 3) the largest crystallization field belongs as a rule to the component with the highest melting point; 4) congruent compounds exhibit a flat maximum; 5)some of the compounds are incongruent; 6) alkali hydroxides and nitrates formed by the same metals give compounds of the type of MOH, MNO_3, where M is an alkali metal. Compounds of this type may be regarded as acid salts of orthonitric acid H_3NO_4, in analogy with orthophosphoric acid H_3PO_4.

SUMMARY

1. Six reciprocal systems of the alkali hydroxide-nitrate exchange decomposition exhibit stratification.

2. Stratification is observed in systems formed by alkali metals which are separated from each other in the periodic system by one, two,or three elements.

3. Systems containing the NO_3^- ion are particularly prone to stratification.

4. Stable pairs of the alkali hydroxide-nitrate exchange decomposition are systems formed from alkali hydroxides with low molecular weight and nitrates with high molecular weight.

The hydroxyl ion generally increases the number of compounds in the systems.

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PROPERTIES OF ACIDS AND BASES IN ACID SOLVENTS

V. POTENTIOMETRIC STUDY OF THE EFFECT OF ANHYDROUS FORMIC ACID ON THE STRENGTH OF ACIDS

A. M. Shkodin, N. A. Izmailov and N. P. Dzyuba

In the preceding papers it was shown that anhydrous formic acid has a high leveling effect on bases [1]. Both strong and extremely weak (in water) bases (pK about 13.8) acquire the same strength in formic acid. The number of substances developing basic properties in acid solvents in comparison with water has been considerably increased, this being bound up with the donor (protogenic) properties of acidic solvents.

Interest attaches to a study of the effect of acid solvents on the strength of acids. In this connection it is a general law that the number of substances possessing acidic properties in solvents with an acid character is considerably smaller than in water. The study of the individual properties of acidic solvents, however, has hitherto been neglected. Acidic solvents vary both in chemical and physical properties and these differences are bound to be reflected in the degree of their influence on the strength of acids.

In a series of papers it was established that acetic acid varies greatly in its effect. Organic acids which have high acidity in water (e.g. trichloracetic acid) become so weak in acetic acid that they do not titrate as acids [2] and exercise a negligible catalytic action [3]. This enabled us to effect fractional titration [2] of the mixture of acids:

$HClO_4$—H_2SO_4, $HClO_4$—HCl, $CH_3C_6H_4SO_3H$—HNO_3.

Formic acid differs markedly from acetic acid in the magnitude of its dielectric constant (57), which determines the electrostatic interaction of ions, as well as in the magnitude of the ionic product (pK_1 of acetic acid is 12.6, that of formic acid is 6.3). It is therefore of interest to study the effect of formic acid on the strength of acids. In the first paper devoted to this problem, Zanninovich-Tessarin [4] arrived, on the basis of cryoscopic measurements, at the conclusion that the dissolved acids become associated in formic acid. The later investigations of Schlesinger [5] showed that anhydrous formic acid has a high dissociating action on salts and acids. An electroconductivity study of hydrochloric acid showed that the degree of dissociation of hydrogen chloride at a molar concentration of 0.0111 is 0.86, while at a concentration of 0.0518 M the value of α is 0.57.

Hammett and Deyrup [6] determined by an indicator method the strength (first constant) of sulfuric acid and benzene sulfonic acid. In this solvent they proved to be strong acids. The same authors obtained a value of $2 \cdot 10^{-3}$ for the second dissociation constant of sulfuric acid.

In the present investigation we attempted to obtain more systematic data for the effect of anhydrous formic acid on the strength of inorganic and organic acids, in view of the theoretical and practical importance of the problem.

EXPERIMENTAL

Anhydrous formic acid was prepared by the previously described method [1,5]. The following acids were studied:

$HClO_4$, HCl, H_2SO_4, $CH_3C_6H_4SO_3H$, CH_3COOH, CCl_3COOH, $CH_2ClCOOH$;

$(NO_2)_3C_6H_2OH$ and $C_6H_4OHCOOH$.

The first two of these were prepared by double decomposition in formic acid:

$$Ba(ClO_4)_4 + H_2SO_4 \rightarrow 2HClO_4 + BaSO_4$$

$$BaCl_2 + H_2SO_4 \rightarrow 2HCl + BaSO_4$$

The starting salts were pure grades, twice recrystallized from water and absolute alcohol. Barium salts were selected because $BaSO_4$ is the least soluble of all barium salts in formic acid. The sulfuric acid was twice distilled over bichromate. Admixture of 1.7 % water to the prepared acid led to a content of 0.02% water in the prepared 0.1 M solutions. Special experiments showed that such an admixture of water does not affect the potential of the quinhydrone electrode, as was also noted by Hammett and Dietz [7]. The precipitates of barium sulfate were not removed as a precaution against absorption of moisture by the solvent during the later operations. As was shown in later experiments, the precipitate had no appreciable effect on the results of titration. The amounts of salts and sulfuric acid were so selected as to give 0.1 M solutions of $HClO_4$ and HCl. In this connection it transpired that the double decomposition between $Ba(ClO_4)_2$ and H_2SO_4 in formic acid does not proceed to completion; instead of the anticipated 0.1 M solution of chloric acid, a mixture of chloric and sulfuric acids is obtained with a total concentration of 0.0885 M, while the proportion of chloric acid is 87%. Solutions of the remaining acids were prepared by dissolving definite weights of the pure anhydrous substances. The technique of investigation consisted in potentiometric titration of 0.1 M solutions of the acids with 0.2 M pyridine solution (pure, freshly distilled material) with a lamp potentiometer. The vessel used for the titration ensured exclusion of atmospheric moisture and was identical with that used in earlier work [1]. The electrochemical cell compound,

$$\text{Pt} \left| \begin{matrix} \text{acid} \\ \text{quinhydrone} \end{matrix} \right| \text{KCl satd.} \Big| \text{KCl satd.} \Big| Hg_2Cl_2 \Big| \text{Hg.}$$

in HCOOH | in H_2O

Titration was performed with quinhydrone and glass electrodes. This was done not only because it was of interest to compare the obtained results and to secure supplementary evidence for the possibility of utilizing the glass electrode in nonaqueous (acidic) media, but also because hydrogen chloride in anhydrous formic acid reacts with quinhydrone and the mixture titrates like the pure solvent. The possibility of utilizing the quinhydrone electrode in formic acid solutions has already been demonstrated [1, 7]. In our work the glass electrode has been repeatedly used for titration in acetic acid. Its potential was rapidly established and remained stable. The possibility of using it in acetic acid solution was demonstrated by the special investigations of Izmailov and Aleksandrova [8]. Attention should be drawn to one special feature of the glass electrode in acid solvents: The potential of the glass electrode during potentiometric titration remains stable for some time (10-15 titration curves), but subsequently the electrode potential is not stable. If the inner solution (Weibel solution) at the electrode is replaced by fresh solution, then the electrode functions again, and the potential is again stabilized but at a value considerably lower than the original potential in otherwise identical conditions.

The plots of titration of the acids at the quinhydrone and glass electrodes exhibit differences in the alkaline region (Fig.1). (We consider solutions containing an excess of $HCOO^-$ ions to be alkaline). The potential jump at the equivalent point is considerably lower for curves plotted with the glass electrode. However, the ratio of the dissociation constants of acids, calculated from the titration curves, was identical for both electrodes. We were thus able, on the basis of glass electrode data, to calculate the dissociation constant of HCl.

Consequently the glass electrode gives a serious error in formic acid in the alkaline region, and this limits its application in formic acid solutions.

Data have been published [5] for 0.1 M solutions of hydrogen chloride in anhydrous formic acid, but we failed to obtain reproducible results for these solutions; titration values varied the whole time even with a reduced amount of HCl, and only after keeping the solution for seven days were reproducible results obtained when titrating half the amount of introduced acid. Since pyridine and HCl form the compounds $Py \cdot 2HCl$ and $Py \cdot HCl$, the half amount may be due to the formation of $Py \cdot 2HCl$. This possibility was not confirmed, however, in titration with sodium formate, and we reached the conclusion that the variable results were due to volatilization of HCl. In the later experiments on HCl titration, therefore, we used 0.05 M solution. The potential of the glass electrode was then satisfactorily reproduced and the equivalence point on the curve was close to the theoretical value. The remaining acids did not introduce any complications.

In Fig. 2 are plotted the titration curves. Their character is that usual for acid-base titrations.

As in the previous cases the effect of formic acid on the strength of the acids was quantitatively evaluated by calculating the dissociation constants with the help of the Roller equation [9].

$$\epsilon = 200\sqrt{K}\sinh\Delta,$$

Fig. 1. Titration curves of toluenesulfonic acid in anhydrous formic acid. 1) With quinhydrone electrode; 2) with glass electrode.

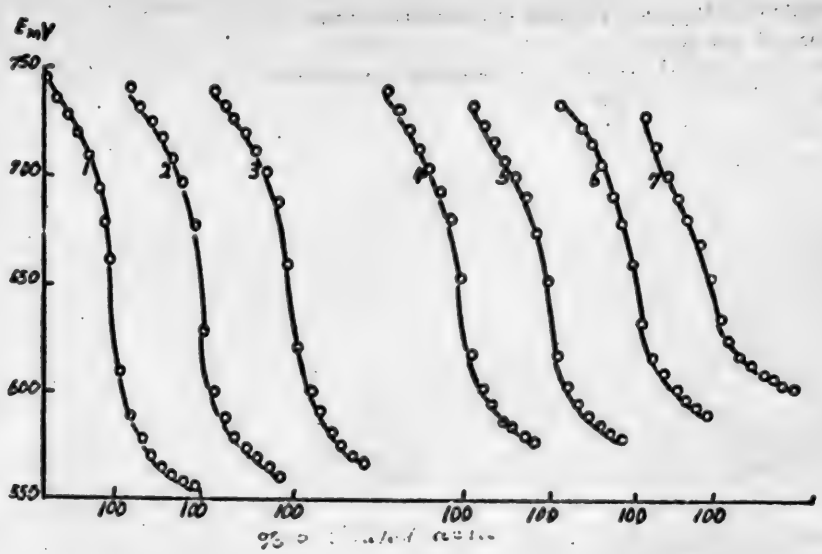

Fig.2. Titration curves of acids in anhydrous formic acid. 1) Chloric; 2) toluenesulfonic; 3) sulfuric with quinhydrone electrode; 4) chloric; 5) toluenesulfonic; 6) sulfuric; 7) hydrochloric, with glass electrode.

where ϵ is the percentage titer error;
Δ is the potential jump in millivolts corresponding to the given titer error multiplied by 0.158;
K is $K_i / C_A K_A$, where K_i is the ionic product of the solvent; K_A is the sought for dissociation constant of the acid; C_A is the salt concentration at the stoichiometric point.

pK_i was calculated from the titration data in accordance with the procedure of Hammett and Dietz [7]. The value of pK_i was corrected for the salt error by the formula

$$pK_i = pK_i' + 2A\sqrt{\mu},$$

where pK_i' is calculated from the titration data;

$A = 0.5(D_{H_2O}/D_{HCOOH})^{3/2}$; D is the dielectric constant; μ is the ionic strength.

No correction is introduced for the error in the degree of dissociation, since the investigated acids and the base used for titration are substantially completely dissociated in formic acid. The resultant value of the ionic product of the solvent in presence of chloric acid (the strongest acid) was equal to 5.77 in the case of the quinhydrone electrode. This value was also taken for calculation of the dissociation constants of acids in the Roller formula cited above.

The obtained pK values for the acids are listed in the table side by side with the pK values of the same acids in acetic acid, calculated by Izmailov [10].

It was found that acetic acid, the chloroacetic acids, salicylic acid and picric acid are so weakened both in formic and acetic acid that they do not titrate as acids. This property may be exploited for fractional titration of mixtures of inorganic and organic acids in formic acid as solvent. Thus the utilization of this solvent both for determination of bases [1] and for fractional titration of acid mixtures widens the potential scope of acid-base titration.

The dissociation constant of HCl in formic acid was calculated from the conductometric data of

TABLE

Dissociation Constants of Acids in Anhydrous Formic Acid and Acetic Acid

Acid	pK_{HCOOH}		pK_{CH_3COOH}
	quinhydrone electrode	glass electrode	
Chloric	0.28	0.56	5.80
Toluenesulfonic	0.34	0.73	–
Sulfuric	0.58	0.94	8.20
Hydrochloric	0.89•	1.23	8.85
Trichloroacetic	–	–	11.46

• pK was calculated from the mean shift of pK of the acids as calculated from the glass and gum hydrone electrode titration curves.

Schlesinger and Martin [5]. The value of the constant for a concentration of 0.0518 M was 0.0385, equivalent to pK = 1.41. Our calculations give a value of pK = 1.23 for 0.05 M HCl. The good agreement for HCl indicates the accuracy of our pK values for the other acids.

Hammett and Deyrup [6] determined the second constant of H_2SO_4 by an indicator method. Since the value of $2 \cdot 10^{-6}$ for the second constant is very close to the value of the ionic product of the solvent, sulfuric acid in formic acid may only be titrated as a monobasic acid. Titration of sulfuric acid in acetic acid, whose ionic product is $2.5 \cdot 10^{-13}$, shows that H_2SO_4 behaves like a monobasic acid in this solvent, probably for the same reason (the value of the second constant of H_2SO_4 is close to the ionic product of acetic acid.

We know that Hantzsch correlated the effect of a solvent on the properties of acids mainly with the chemical transformations of acids under the influence of the solvent due to reaction of acid with solvent. Hantzsch relegated the physical properties of the solvent to a secondary place. Comparison, however, of the obtained data for acid strengths in acidic solvents (formic and acetic acids) is indicative of the very important role of the dielectric constant of the solvent. Inorganic acids in formic acid (DC = 57) are considerably weaker than in acetic acid (DC = 6). Whereas acetic acid alters the strength of inorganic acids to such a degree that some of them can be fractionally titrated, the inorganic acids which are strong in water remain strong in formic acid, although they become somewhat weaker than in water.

SUMMARY

1. A study was made by the method of potentiometric titration of the effect of anhydrous formic acid on the strength of inorganic and organic acids (chloric, sulfuric, hydrochloric, toluenesulfonic, trichloroacetic, monochloroacetic, picric, acetic and salicylic).

2. It was shown that inorganic acids remain strong in anhydrous formic acid; formic acid differs from acetic acid in not possessing a modifying effect on the strength of inorganic acids, due to the high dielectric constant of formic acid. Organic acids become so weak in formic acid that they do not titrate like acids. This characteristic may be utilized for fractional titration of mixtures of inorganic and organic acids.

3. The dissociation constants of chloric, sulfuric, hydrochloric and toluenesulfonic acids were calculated from the titration data.

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THE MOBILITY OF HYDROGEN IN SOME ORGANOSILICON COMPOUNDS.

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Isotopic exchange of atoms in C–H bonds is strongly hindered or does not take place at all. An appreciable velocity is only observed when this bond is weakened by appropriate substituents, reagents or catalysts. In discussing the hindrance to exchange at C–H bonds, A. I. Brodsky [1] suggested that rapid hydrogen exchange only proceeds in presence of a free electron pair at an atom which is not the exchanging hydrogen (N, O, Cl, etc.). In such cases the exchange reaction is associated with an insignificant activation energy, since activation is not required for preliminary breaking of the element-hydrogen bond. Here the addition of deuterium and the removal of hydrogen occur simultaneously.

The carbon in compounds is surrounded by an electron shell not possessing free electron pairs to which the deuterium of a suitable donor might be able to add on at a greater speed than that at which the rupture of one of the C–H bonds takes place. Consequently this exchange calls for a high activation energy and proceeds relatively slowly and only when the C–H bond is weakened. These speculations are consistent with the marked inhibition of hydrogen exchange in H–H and B–H bonds, which are likewise not surrounded by free electron pairs, and in the ammonium ion [2] where, in contrast to ammonia or amines, all the electron pairs are bonded toundan atom of nitrogen. In silicon compounds, as in compounds of its analog (carbon), all the electron pairs are similarly bonded. Thus the Si–H bond in organosilicon compounds should resemble the C–H bond in exchange susceptibility, and the study of isotopic exchange in these compounds may serve to confirm the correctness of the foregoing ideas. Such an investigation is also of interest in itself since it has not previously been undertaken.

In this investigation hydrogen exchange was studied in the Si–H bonds of the silanes $HSi(C_2H_5)_3$ and $HSi(C_6H_5)_3$ and of triethoxysilane $HSi(OC_2H_5)_3$. The hydrogen donors were heavy water, heavy ethyl alcohol C_2H_5OD, and heavy diethylamine $DN(C_2H_5)_2$.

The choice of the organosilicon compounds was dictated by their superior stability compared with unsubstituted silanes, by the presence of only one Si–H bond, and by the presence of substituents with differing degrees of electronegativity.

EXPERIMENTAL

The starting material, silicochloroform, $HSiCl_3$, was prepared by the action of dry hydrogen chloride on silicon at 300° [3]. After fractionation the product had b.p. 32°. Yield 44%.

Triethylsilane $HSi(C_2H_5)_3$ was prepared by reaction of silicochloroform with a Grignard reagent [4]. After fractionation the product had b.p. 107-108° and d_4^{20} 0.7301. Yield 52% of theory.

Under the action of alcoholic potassium hydroxide it is converted into triethylsilanol with b.p. 154-156° and d_4^{20} 0.8597; when boiled with 30% aqueous alkali it forms hexaethyldisiloxane with b.p. 223°; when the latter is heated with alcoholic alkali it is transformed into the same triethylsilanol.

Triphenylsilane $HSi(C_6H_5)_3$ was prepared by the same method [5]. After distillation under reduced pressure (b.p. 180° at 15 mm) the product solidified as a colorless crystalline mass with m.p. 36°. Yield 67%. Conflicting data about triphenylsilane have appeared in the literature. Ladenburg [6] claimed to have prepared triphenylsilane in the form of crystals with m.p. 200-203° from the corresponding bromide by the action of an alkyl zinc in a sealed tube. Kipping and Murray [7] prepared triphenylsilane by destructive distillation of cyclosilicotetrane $Si_4(C_6H_5)_8$ in the form of an oil which did not solidify at 0° and which was converted by HBr into $(C_6H_5)_3SiBr$; the latter with 5% NaOH gave triphenylsilanol. Reynolds, Bigelow, and Kraus [5], whose method we repeated for the synthesis, considered the results of the earlier authors to be erroneous and that Kipping had only obtained a very impure triphenylsilane as evidenced by the oily form.

Andrianov and Sobolevsky recently [8] drew attention to the need for checking the data on this compound. Our results have confirmed that Reynolds and co-workers actually prepared pure triphenylsilane.

For the purpose of identification of our preparation, it was converted by boiling with alcoholic alkali into a substance which after three recrystallizations from ligroin melted at 151°. It did not depress the melting point of triphenylsilanol prepared from $SiCl_4$ and $MgBrC_6H_5$ [9]. Digestion of our preparation with 30% aqueous alkali gave hexaphenyldisiloxane with m.p. 222°, which with alcoholic alkali is converted into the same triphenylsilanol.

Triethoxysilane $HSi(OC_2H_5)_3$ was prepared in benzene solution from $HSiCl_3$ and absolute alcohol [10]. The fractionated product had b.p. 134° and d_4^{20} 0.8753; yield 43% of theory.

In the work in question [10] it was found that an increase in the period of standing of the reaction mixture led to an increase in the amount of by-product $Si(OC_2H_5)_4$ at the expense of the main product. This has been ascribed to the reactions:

$$HSi(OC_2H_5)_3 + HCl \longrightarrow ClSi(OC_2H_5)_3 + H_2;$$

$$ClSi(OC_2H_5)_3 + C_2H_5OH \longrightarrow Si(OC_2H_5)_4 + HCl.$$

According to the same authors, however, the yields did not fall when HCl was passed through in a nitrogen stream. We found that pure $HSi(OC_2H_5)_3$ is converted to a very large extent into $Si(OC_2H_5)_4$ when heated in sealed glass ampoules with alcohol. Lowering of the temperature increases the amount of unreacted material. The reaction proceeds to a slight extent even in the cold. When the ampoules are opened a brown gas escapes which had been dissolved under pressure in the liquid. For conclusive demonstration of the interaction of $HSi(OC_2H_5)_3$ with alcohol, we heated two ampoules at 100° for 125 hours. The first ampoule contained pure $HSi(OC_2H_5)_3$, which remained unchanged after heating; the second contained $HSi(OC_2H_5)_3$ and absolute alcohol. When the latter was heated about one-half of the triethoxysilane was converted into $Si(OC_2H_5)_4$ with b.p. 165-166° and d_4^{20} 0.9308. Hence $HSi(OC_2H_5)_3$ reacts with alcohol according to the nucleophilic scheme:

$$HSi(OC_2H_5)_3 + C_2H_5OH \longrightarrow H_2 + Si(OC_2H_5)_4.$$

Isotopic exchange was conducted in sealed glass ampoules placed in a thermostat. Conditions were selected in which the silanes were relatively stable. Water forms a two-phase system with triethylsilane and triphenylsilane. With alcohol the first forms a homogeneous solution; with diethylamine both give homogeneous solutions. In some experiments the exchange with water was performed in homogeneous pyridine and dioxan solution. Triethoxysilane forms a homogeneous solution with alcohol. After completion of exchange the components were separated. Since the silanes contain a large numb of unexchanged hydrogen atoms per atom of exchange hydrogen, the relative chang of density of alcohol or water, even with complete exchange would be small. After the exchange, therefore, the deuterium content of the silane was determined. The material was calcined and the deuterium content of the resultant water was determined by the flotation method. The deuterium content of the alcohol and diethylamine was similarly determined. The experimental results are presented in Tables 1 and 2.

TABLE 1

Isotopic Exchange of Hydrogen in Triethylsilane

Donor	Catalyst	Temp.	Duration (hrs)	Water density (in γ units)		
				initial*	from combustion	
					complete exchange of one hydrogen; calculated	found
D_2O	–	116°	51	2670	165	0
D_2O	H_2SO_4	116	49	2670	163	0
D_2O	KOH	116	70	2670	164	4
D_2O + pyridine .	–	116	50	22000	1220	7
D_2O + dioxan	–	100	12	3500	212	15
D_2O + dioxan	H_2SO_4	100	15	3500	211	6
C_2H_5OD	–	100	25	7000	296	0
C_2H_5OD	CH_3COONa	116	117	7000	346	0
C_2H_5OD	$KHSO_4$	118	146	7000	340	0
$DN(C_2H_5)_2$	–	78	18	16130	656	0

* In the case of alcohol the D content of the hydroxyl group; in the case of diethylamine the D content of the NH group.

TABLE 2

Isotopic Exchange of Hydrogen in Triphenylsilane and Triethoxysilane

Donor	Catalyst	Temp.	Duration (hours)	Water density (in γ units)		
				initial*	from combustion	
					complete exchange of one hydrogen; calcd.	found
Triphenylsilane						
D_2O	–	18	335	6550	306	5
D_2O	–	90	15	6550	250	7
D_2O	–	103	20	6500	306	12
D_2O	–	118	71	2670	164	7
D_2O	H_2SO_4	103	20	6550	332	6
D_2O	H_2SO_4	118	69	2670	165	0
D_2O	NaOH	103	18	6500	340	13
D_2O + dioxan .	–	100	11	3500	211	4
D_2O + dioxan .	H_2SO_4	100	15	3500	212	0
$DN(C_2H_5)_2$ . . .	–	20	50	16130	738	8
$DN(C_2H_5)_2$ . . .	–	78	10	16130	728	10
Triethoxysilane						
C_2H_5OD	–	20	49	7000	350	2

The triethylsilane was separated from water in a separating funnel, dried over $CaCl_2$ and fractionated. Difficulties accompanied its separation from alcohol because an azeotropic mixture boiling at about 65° is formed. Consequently as soon as the absence of exchange with water had been established, the alcohol was washed out with water. The pyridine and dioxan were likewise washed out. After exchange with diethylamine, the triethylsilane was fractionated, washed with water, and dried over $CaCl_2$.

The water or alcohol was distilled off from triphenylsilane and triethoxysilane with benzene, as suggested by Dean and Stark, or in vacuum. Diethylamine was separated by distillation. In all cases the $HSi(C_6H_5)_3$ was purified by vacuum distillation.

$HSi(C_2H_5)_3$ at room temperature in homogeneous alcoholic or aqueous dioxan solutions decomposes with loss of hydrogen when a small quantity of alkali is added. The OC_2H_5 ion has the same effect. This is not observed in pyridine. The catalyst selected for experiments on alkaline catalysis during exchange with heavy alcohol was therefore the weak base CH_3COONa.

$HSi(C_6H_5)_3$ which has been homogenized reacts even more vigorously with alkali, losing hydrogen even in aqueous pyridine solution. $HSi(OC_2H_5)_3$ reacts in a beaker even with a base such as alcohol (see above).

The data presented, and certain other data, have limited the possibility of conducting exchange experiments in the conditions specified in the tables.

EVALUATION OF RESULTS

From the above results we can conclude that even after prolonged heating with acid or alkali not one of the three investigated silanes undergoes exchange with heavy water, heavy alcohol or heavy diethylamine. The negligible content of deuterium found in the silanes in some experiments does not exceed a few percent of the amount anticipated for complete exchange and may be ascribed to retention of traces of water.

The analogous carbon compounds exhibit the same behavior in respect to exchange. Triphenylmethane does not exchange hydrogen with heavy water after 144 hours at 100° in presence of alkali [11]; isobutane only gives a slow exchange with 100% sulfuric acid containing tritium [12]. The exchange of an orthoformic ester has not been investigated.

In conformity with its position in the periodic system, silicon is less electronegative than carbon. The electronegativity of carbon is greater than that of hydrogen, and this brings about partial polarization of the $\overline{C}-\overset{+}{H}$ bond susceptible to electrophilic reactions. When electrons are removed by electronegative substituents, ionization of the hydrogen may occur. Conversely, the electronegativity of silicon is less than that of hydrogen, and hence the bond is polarized in the reverse direction: $\overset{+}{Si}-\overline{H}$. In this case exchange by an electrophilic mechanism is not very probable, and this also makes nucleophilic substitution improbable. Thus, compounds of the type of R_3SiH react nucleophilically toward caustic alkali, amides of metals, alcoholates, etc. The

* In the case of alcohol the D content of the hydroxyl group; in the case of diethylamine the D content of the NH group.

concept of nucleophilic substitution reactions in silicon compounds is consistent with the possibility of complex formation with probable completion of the outer electron shell of Si to a value of 12 (SiF_6^{--}; salts of siliconium).

In compounds of the R_3SiH type electronegative substituents (R= C_6H_5, OC_2H_5), which do not cause ionization, increase the positive charge on the Si atom, thereby accelerating the reaction of nucleophilic substitution of the type of

$$\equiv Si{-}H + \cdot\overline{OR'} \longrightarrow \equiv Si{-}OR' + \overline{H}; \overline{H} + \overset{+}{H} \longrightarrow H_2 \ (R' = H \text{ or alkyl}).$$

In the case of $HSi(C_6H_5)_3$ the OH ion concentration of aqueous pyridine solution is adequate for this reaction, while $HSi(OC_2H_5)_3$ reacts even with a weak base such as alcohol. In the light of this reaction we can understand the notable increase of yield in the synthesis of trialkoxysilanes in passing from ethyl to butyl [10]. Actually the increasing chain length of the alkyl radical increases its positive inductive effect, thereby reducing the positive charge on the silicon atom of the $\overset{+}{Si}{-}\overline{H}$ bond, and in turn the susceptibility to the nucleophilic substitution reaction. Fluorine is even more negative than ethoxyl, and consequently the positive charge on the silicon in $HSiF_3$ is greater than in $HSi(OC_2H_5)_3$ and $HSiCl_3$. The consequence of this is that when $HSiF_3$ reacts with alcohol [13] we obtain only $Si(OC_2H_5)_4$ and no $HSi(OC_2H_5)_3$:

$$2HSiF_3 + 4C_2H_5OH \longrightarrow Si(OC_2H_5)_4 + H_2SiF_6 + H_2.$$

Similarly $HSiCl_3$ (chlorine is more positive than fluorine) reacts with water in the cold to give polymeric silicoformic anhydride $\left(H{-}Si(=O){-}O{-}Si(=O){-}H\right)_x$, which contains the SiH group, while $HSiF_3$ gives silicic acid $\left(HO{-}Si(=O){-}OH\right)_x$.

The possibility of a radical mechanism cannot be excluded for hydrogen exchange in the Si–H bond if we remember that its energy is 12 kcal lower than that of the C–H bond. Up to now no convincing evidence has been obtained of a nucleophilic mechanism of hydrogen exchange of isotopes, for which a source of H^- ions is necessary. The probability of such a mechanism is limited by the low stability of the negative hydrogen ion or of the intermediate hydride complexes.

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SUMMARY

1. Hydrogen exchange is shown not to take place in the compounds $HSi(C_2H_5)_3$, $HSi(C_6H_5)_3$ and $HSi(OC_2H_5)_3$ with D_2O, C_2H_5OD and $DN(C_2H_5)_2$, even under prolonged heating in presence of acids and bases.

2. These data bring the Si–H bond within the terms of A. I. Brodsky's earlier theory of isotopic hydrogen exchange.

3. Reaction was found to occur between triethoxysilane and alcohol with hydrogen exchange at the ethoxy group.

4. Considerations are put forward which explain the absence of exchange in the above-mentioned compounds and some peculiarities of substitution reactions at Si–H bonds.

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REACTIONS OF HYDROXIDES OF ARYL MERCURY

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In our previous paper [1] on the photochemical reactions of phenylmercury hydroxide in various solvents, a theory was put forward for the dissociation of the hydroxide into the hydroxyl radical and the phenylmercury radical. The latter radical reacted with the halogen contained in the solvent to form phenylmercury halide; in halogen-free solvents (alcohol, ethyl cellosolve) metallic mercury separated out and benzene was formed; in benzene solution diphenyl was formed. Separation of mercury may be considered to proceed by one of two routes: 1) Directly from the phenylmercury radical; or 2) through intermediate formation of diphenylmercury which reacts further by the usual scheme [2]. Cleavage of Hg from the C_6H_5Hg radical is extremely probable. We know that methylmercury prepared by electrolysis rapidly breaks down at the ordinary temperature into mercury and dimethylmercury [3].

In order to resolve this problem, experiments were conducted with phenylmercury hydroxide in solution in ethyl cellosolve and benzene. The reaction did not proceed to the end; irradiation was stopped when mercury began to separate. Diphenylmercury was found in solution in quantity equivalent to the separated mercury (Table 2, experiments 1 and 2).

$$C_6H_5HgOH + h\nu \longrightarrow C_6H_5Hg^{\cdot} + OH^{\cdot}$$
$$2C_6H_5Hg^{\cdot} \longrightarrow (C_6H_5HgHgC_6H_5) \longrightarrow (C_6H_5)_2Hg + Hg.$$
$$(C_6H_5)_2Hg + h\nu \longrightarrow C_6H_5Hg^{\cdot} + C_6H_5^{\cdot} \text{ etc.}$$

It may here be permissible to suggest a symmetrization reaction of the phenylmercury hydroxide by analogy with the symmetrizations of unsymmetrical mercury derivatives. With a view to checking this hypothesis experiments were performed on the thermal decomposition of the hydroxide in methanol solution. Among the reaction products apart from metallic mercury, benzene and formaldehyde, was found diphenylmercury in amount of 12-25% (Table 1). These data conclusively point to symmetrization of phenylmercury hydroxide during thermal reactions.

However, if the symmetrization of the hydroxide were to be effected in presence of ultraviolet light, then in halogen-containing solvents the yield of phenylmercury halide should not exceed 50%. Actually up to 80% of phenylmercury iodide was obtained in the photochemical reaction of phenylmercury hydroxide in a mixture of benzene and iodobenzene. We can therefore assume that diphenylmercury is formed photochemically by the above scheme.

In this investigation a study has also been made of the photochemical reactions of arylmercury hydroxides containing various substituents in the benzene ring. As with phenylmercury hydroxide the reactions in ethyl cellosolve proceed according to the general equation:

$$RC_6H_4HgOH + HOCH_2CH_2OC_2H_5 + h\nu \longrightarrow C_6H_5R + Hg + H_2O + 2CH_3CHO,$$
where R = o- and p-CH_3; n-$(CH_3)_2N$.

Mesitylmercury hydroxide reacts in the same way (Table 2, experiments 3-6).

In benzene solution the hydroxides of o- and p-tolylmercury give the same products as phenylmercury hydroxide in toluene: methyldiphenyl, water and mercury, i.e. substitution takes place in the benzene ring (Table 2, experiments 7 and 8).

Mesitylmercury hydroxide did not react with benzene even after very prolonged irradiation (200 hours). The difference between mesitylmercury hydroxide and the other hydroxides investigated was also reflected in its photochemical reactions with chloroform and carbon tetrachloride. The mesitylmercury chloride anticipated by analogy was not detected. Mesitylene was found in the chloroform solution and chloromesitylene in the carbon tetrachloride solution. An organomercury compound insoluble in common solvents was obtained in the latter experiment and must have been formed by cleavage of the hydroxyl from the $(CH_3)_3C_6H_2Hg^{\cdot}$ radical.

In both solvents mercuric chloride and calomel were formed due to the chlorinating action of the solvent on mercury under irradiation. These characteristics of the mesityl radical were previously manifested in the photochemical reactions of dimesityl mercury [4] (Table 2, experiments 9 and 10).

TABLE 1

Substance used		Period of heating (hours)	Temp. of heating (°C)	Obtained					
				mercury		diphenyl mercury		benzene	formaldehyd
C_6H_5HgOH (g)	CH_3OH (ml)			g	%	g	%	(g)	(g)
2.5	20	70	180-185	1.25	73.6	0.75	24.9	0.08	0.2
3.0	20	24	200	1.78	88.2	0.45	12.4	0.36	0.3

Note. In these experiments benzene was identified by conversion to m-dinitrobenzene; formaldehyde was identifie in the form of the dimedon derivative with m.p. 188°.

TABLE 2

Expt. No.	Materials taken				Irradiation period (hours)	Obtained	
	Hydroxides		Solvents			unchanged hydroxide	
	Formula	Quantity (g)	Name	Quantity (ml)		g	%
1	C_6H_5HgOH	3	Ethyl cellosolve	10	3	2.5	83.3
2	C_6H_5HgOH	2	Benzene	20	25	1.4	70.0
3	o-$CH_3C_6H_4HgOH$.	1.2	Ethyl cellosolve	15	18	–	–
4	p-$CH_3C_6H_4HgOH$.	2	Ethyl cellosolve	15	22	–	–
5	$(CH_3)_3C_6H_2HgOH$.	1.5	Ethyl cellosolve	15	10	–	–
6	$(CH_3)_2NC_6H_4HgOH$	2	Ethyl cellosolve	4	12	–	–
7	o-$CH_3C_6H_4HgOH$.	1.8	Benzene	15	60	0.45	25.0
8	p-$CH_3C_6H_4HgOH$.	1.8	Benzene	25	100	0.55	30.6
9	$(CH_3)_3C_6H_2HgOH$.	1.5	Chloroform	12	70	–	–
10	$(CH_3)_3C_6H_2HgOH$.	1.3	Carbon tetrachloride	15	60	–	–

TABLE 3

Expt. No.	taken					Duration of irradiation (in hours)
	C_6H_5HgOH	Solvent				
		1st component		2nd component		
		name	(ml)	name	(ml)	
1	3	Benzene	10	Iodobenzene	10	80
2	2	Benzene	20	Ethyl cellosolve	5	15
3	1.8	Benzene	25	Isopropyl alcohol	5	80
4	2.5	Benzene	20	Carbon tetrachloride	12	130

We were unable to clarify the reaction of p-dimethylaminophenylmercury with carbon tetrachloride. Mercury, mercuric chloride and calomel were found after irradiation of the solution; a dye was also obtained, probably a member of the triphenylmethane series, which gave violet solutions in acetone and benzene. The color changed to green under the action of acids.

We see from the experimental data that the behavior of the radicals formed on photolysis depends on the nature of the substituent, i.e., whether reactions involving removal of hydrogen or halogen take place, while in aromatic solvents substitution reactions take place. It therefore appeared of interest to perform photochemical reactions of phenylmercury hydroxide in a mixture of two solvents in order to establish the direction of the reaction in a given case. Phenylmercury iodide, diphenyl and water were formed in the photochemical reaction of phenylmercury hydroxide with iodobenzene and benzene. On the basis of the obtained data we may suggest that benzene entered into reaction with hydroxyl to form the phenyl radical:

$$C_6H_5HgOH + C_6H_5I + h\nu \longrightarrow C_6H_5HgI + C_6H_5C_6H_5 + H_2O.$$

Mercury separated when the reaction was carried out in a mixture of benzene and ethyl cellosolve; acetaldehyde was detected and a small amount of diphenyl.

The irradiation of a solution of phenylmercury hydroxide in a mixture of benzene and carbon tetrachloride led to separation of phenylmercury chloride, calomel, mercuric chloride, hexachloroethane, water and benzotrichloride, (the latter was identified by conversion to benzoic acid). Formation of benzotrichloride proceeds either at the expense of entry of the CCl_3 radical into the benzene ring, as happened in the studies of Nesmeyanov, Pecherskaya and Uretskaya [5], or as the result of addition of two radicals – CCl_3 and phenyl (Table 3).

We thus see that photochemical reactions in a mixture of solvents proceed according to complex schemes. The course of the reaction may be accurately followed with the help of labeled atoms.

EXPERIMENTAL

1. Thermal reaction of phenylmercury hydroxide in methyl alcohol. The reaction mixtures were heated

TABLE 2

Product	Obtained								Other products
	Hg		$HgCl_2$		Hg_2Cl_2				
Formula	g	%	g	%	g	%	g	%	
$(C_6H_5)_2Hg$	0.13	–	0.10	–	–	–	–	–	
$(C_6H_5)_2Hg$	0.07	–	0.09	–	–	–	–	–	0.05 g diphenyl
$C_6H_5CH_3$	0.30	82.6	0.67	87.0	–	–	–	–	Acetaldehyde
$C_6H_5CH_3$	0.45	76.1	1.25	96.1	–	–	–	–	Acetaldehyde
$C_6H_3(CH_3)_3$	0.40	75.4	0.82	92.1	–	–	–	–	Acetaldehyde
$C_6H_5N(CH_3)_2$	0.60	65.0	1.10	92.4	–	–	–	–	Acetaldehyde
$o\text{-}CH_3C_6H_4C_6H_5$	0.60	65.0	0.75	91.4	–	–	–	–	Water
$p\text{-}CH_3C_6H_4C_6H_5$	0.30	84.7	0.65	80.2	–	–	–	–	Water
$C_6H_3(CH_3)_3$	0.41	77.3	–	–	0.28	23.4	0.78	74.1	C_2Cl_6
$C_6H_2Cl(CH_3)_3$	0.17	32.8	–	–	0.15	14.2	0.30	34.8	C_2Cl_6, organomercury compound

TABLE 3

C_6H_5HgX		Obtained: Product		Hg		$HgCl_2$		Hg_2Cl_2		Other products
g	%	Formula	g	g	%	g	%	g	%	
3.2	80.1	$(C_6H_5)_2$	0.30	–	–	–	–	–	–	Water
–	–	$(C_6H_5)_2$	0.08	1.3	95.1	–	–	–	–	Acetaldehyde
–	–	$(C_6H_5)_2$	0.01	0.22	18.0	–	–	–	–	Acetone
0.50	18.8	$C_6H_5CCl_3$	0.09	–	–	0.88	44.1	0.70	34.9	Hexachloroethane

in sealed ampoules. The reaction products were identified by determination of their boiling points and of the melting points in admixture with pure substances. The experimental results are set out in Table 1.

2. Photochemical reactions of arylmercury hydroxides in solutions. Experiments were performed in quartz test tubes which were irradiated at room temperature with a PRK-2 quartz mercury lamp. The experimental results are set out in Table 2.

Notes. 1. The percent yield of mercury and methyldiphenyl in experiments 7 and 8 were calculated on the basis only of the hydroxide entering into reaction.

2. The o- and p-methyldiphenyls in these reactions were identified by oxidation to the corresponding diphenyl carboxylic acids whose constants were then determined.

3. The products obtained in experiments 3-6 were identified by boiling point determinations

(Sivolobov's method). Subsequently the toluene (in experiments 3 and 4) was oxidized to benzoic acid with m.p. 121°; mesitylene was nitrated to 2,4,6-trinitro-1,3,5-trimethylbenzene with m.p. 233°; dimethylaniline was identified as its picrate, m.p. 162°.

4. Mesitylene and chloromesitylene (in experiments 9 and 10) were also identified by nitration to 2,4,6-trinitro-1,3,5-trimethylbenzene with m.p. 178°.

5. Mercuric chloride (Table 2, experiments 9 and 10; Table 3, experiment 4) was washed out with hot water and precipitated in the form of mercury sulfate. Calomel was identified by its qualitative reactions.

6. The melting points of hexachloroethane were determined in sealed capillaries (m.p. 183°).

3. Photoreactions of phenylmercury hydroxide in mixed solvents. The experimental results are presented in Table 3.

Notes. 1. The reaction products (columns 8 and 9) were identified by mixed melting point determinations.

2. The molecular weight of the obtained diphenyl (expt. 1) was found to be 155.4 (calculated 154).

3. Benzotrichloride (expt. 4) was isolated by conversion into benzoic acid (m.p. 121°), which was then titrated with alkali.

SUMMARY

1. Breakdown of the $C_6H_5Hg^{\cdot}$ radical when phenylmercury hydroxide is irradiated with ultraviolet light proceeds through formation of diphenylmercury.

2. The photoreactions of the hydroxides of o- and p-tolylmercury, mesitylmercury, and p-dimethylaminophenylmercury in ethyl cellosolve were investigated. These reactions proceeded in a similar manner to the reactions of phenylmercury hydroxide.

3. The reactions of o- and p-tolylmercury hydroxides in benzene were investigated. These photoreactions proceed with formation of methyldiphenyl due to a substitution reaction.

4. The photoreactions of mesitylmercury hydroxide were investigated. Irradiation of this compound in chloroform solution leads to formation of calomel, mercuric chloride, mesitylene and hexachloroethane. In carbon tetrachloride the products are calomel, chloromesitylene, hexachloroethane and an organomercury compound.

5. The following results were obtained in the photoreaction of phenylmercury hydroxide:

a) In benzene-iodobenzene mixture, phenylmercury iodide, diphenyl and water were obtained.

b) In benzene-ethyl cellosolve mixture, mercury, diphenyl and acetaldehyde were obtained.

c) In a mixture of benzene and carbon tetrachloride, the products were phenylmercury chloride, calomel, mercuric chloride, hexachloroethane and benzotrichloride.

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** See Consultants Bureau translation, p. 717.

THE PROBLEM OF THE STRUCTURE OF GUSTAVSON'S HYDROCARBON

III. THE ACTION OF ZINC DUST ON TETRAHALONEOPENTANES

Ya. M. Slobodin and I. N. Shokhor

As far back as 1896, G. G. Gustavson [1-3] showed that zinc dust acts on tetrabromoneopentane to form a hydrocarbon with the composition C_5H_{10}. Later investigations of Demyanov, Favorsky, Filippov Whitmore and others established that Gustavson's hydrocarbon is a mixture consisting of methylenecyclobutane and 2-methyl-1-butene. Additional factors may lead to the formation, apart from the above-mentioned compounds, of spiropentane and very small amounts of 1,1-dimethylcyclopropane. Thus when tetrabromoneopentane is treated with zinc dust in aqueous ethanol, a mixture is formed which consists solely of methylenecyclobutane and 2-methyl-1-butene [4]. In aqueous methanol there is formed, in addition, a small quantity of spiropentane [5]. Addition of zinc bromide shifts the reaction in the direction of preferential formation of methylenecylcobutane [6].

Hass and McBee [7] investigated the conditions of formation of cyclopropane from 1,3-dichloropropane and found that optimum yields (95%) are obtained by cleavage of halogen in aqueous ethanol in presence of sodium carbonate and sodium iodide. The same results are obtained on substituting anhydrous acetamide for aqueous ethanol. It was also found that the substitution of one or both atoms of chlorine in 1,3-dichloropropane by iodine leads to better yields of the hydrocarbon. It is evident that the role of sodium iodide is to introduce iodine ions which undergo double decomposition with the molecule of 1,3-dichloropropane. The sodium carbonate serves to regenerate the iodine ions formed by reaction of the weakly dissociated zinc iodide.

The application of these conditions to tetrabromoneopentane led to the formation of spiropentane [5]. Dehalogenation in fused acetamide (170-180°) in presence of sodium carbonate and sodium iodide gave a hydrocarbon in 38% yield and with a spiropentane content of 47-60%. Using the same additives in aqueous ethanol, the yields of hydrocarbon were 78-79%. It contained 28% spiropentane, 56% methylene-cyclobutane, 18% 2-methyl-1-butene and about 1-3% of 1,1-dimethylcyclopropane [8]. Consequently, the conditions favoring closure of the cyclopropane ring also promote the formation of spiropentane.

In the present investigation a study was made of the effect of the nature of the halogen atom (Cl, Br, I) on the composition of the hydrocarbon mixture formed by the action of zinc dust on tetrahaloneopentanes in dilute alcohol and in dilute acetamide with and without additions of sodium carbonate and sodium iodide. In order to avoid secondary reactions the volatile products were immediately distilled off from the reaction mixture.

The composition of the hydrocarbon mixture was determined in each experiment with the help of Raman spectra. Visual comparison of the intensities of the spectral lines enabled the composition of the mixture to be determined to an accuracy of only up to 10%, but even this relatively rough analysis permitted certain regular characteristics in the series of tetrahalo derivatives of neopentane to be established.

No dehalogenation occurred when zinc dust acted on tetrachloroneopentane in presence of sodium carbonate in dilute alcohol, and the whole of the starting material was recovered unchanged. When the alcohol was replaced by ethylene glycol the reaction proceeded very sluggishly even at 180-190°. A minute amount of a hydrocarbon and an unsaturated chloride with b.p. about 80° were formed. Nearly half of the original material was recovered unchanged. A definite reaction took place only when using anhydrous acetamide. In presence of sodium carbonate at 170-180° a hydrocarbon mixture was obtained which boiled at 33-42°. The Raman spectrum contained lines whose frequencies coincided with those attributed in the literature to mixtures of spiropentane, methylenecyclobutane and 2-methyl-1-butene [5,11,12]. The composition of the hydrocarbon mixture was methylenecyclobutane 80-85%, spiropentane 10%, 2-methyl-1-butene 5-10%.

In presence of sodium carbonate and sodium iodide, the content of spiropentane, as was to be expected, rose to 30-40%, that of 2-methyl-1-butene rose to 10-20%, and the methylenecyclobutane content fell to 50% (Table 1).

TABLE 1

Dehalogenation of Tetrachloroneopentane

Method of preparation of the hydrocarbon	Total yield of hydrocarbons (%)	% Content		
		spiropentane	methylene-cyclobutane	2-methyl-1-butene
In acetamide in presence of sodium carbonate. .	40	10	80-85	5-10
In acetamide in presence of sodium carbonate and sodium iodide	40-50	30-40	50	10-20

TABLE 2

De halogenation of Tetrabromoneopentane

Method of preparation of hydrocarbon	Total yield of hydrocarbons (%)	% Content			
		spiropentane	methylene-cyclobutane	2-methyl-1-butene	1,1-dimethyl cyclopropan
In aqueous ethanol (Gustavson's method [13].	80	–	80-90	10-15	–
In aqueous ethanol in presence of sodium carbonate and sodium iodide [8]. . . .	78-89	24-28	54-58	13-18	1-3
In acetamide in presence of sodium carbonate	40	20-30	50-60	10-20	–
In acetamide in presence of sodium carbonate and sodium iodide [8].	38	47-60	36-10	17-30	–

Results of dehalogenation of tetrabromoneopentane are set out in Table 2.

Tetraiodoneopentane in aqueous alcohol reacts with zinc dust very slowly. In fused acetamide in presence of sodium carbonate and sodium iodide a mixture of hydrocarbons containing 50% spiropentane is formed. The amount of spiropentane does not change even when the reaction is performed in acetamide without sodium carbonate and sodium iodide (Table 3).

TABLE 3

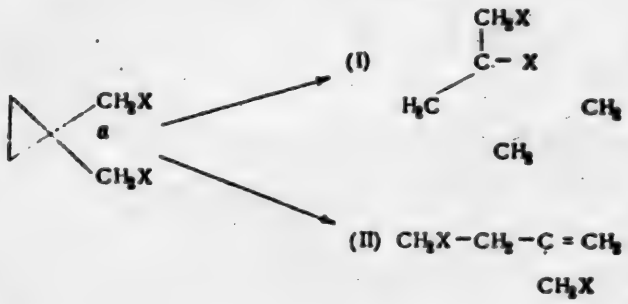
Dehalogenation of Tetraiodoneopentane

Method of preparation of the hydrocarbon	Total yield of hydrocarbons(%)	% Content		
		spiropentane	methylene-cyclobutane	2-methyl-1-butene
In acetamide in presence of sodium carbonate and sodium iodide.	80	50	40	10
In acetamide without additives	80	50	25	25

A comparison of the tabulated data permits the conclusion to be drawn that in anhydrous acetamide in presence of sodium carbonate the yields of spiropentane increase as we pass from tetrachloro- to tetraiodoneopentane, the tetrabromo-compound occupying an intermediate position. Additions of sodium carbonate considerably increase the yields of spiropentane from tetrachloro- and tetrabromoneopentanes. Addition of sodium carbonate has no influence on the yield of spiropentane from tetraiodoneopentane, which fact confirms its role as a medium promoting the regeneration of iodine ions in the reaction. Yields of 2-methyl-1-butene increase as we pass from the tetrachloro- to the tetraiodo- compound. It may be suggested that the increase in yields of spiropentane is related to the magnitude of the atomic radii of the halogens.

1,1-Dihalodimethylcyclopropane must be an intermediate product of the dehalogenation of the tetrahaloneopentanes. The formed trimethylene ring with a valency angle of 60° causes expansion of the outer valency angle [14,15]. Thus, we know from electronographic data that the H-C-H angle in cyclopropane is 118° [14]. The enlargement of the valency angle α in 1,1-dihalodimethylcyclopropane greatly hinders the closure of the second three-membered ring and in turn hinders the formation of spiropentane.

In addition, the formed 1,1-dihalodimethylcyclopropane, possessing a well-known isomerization tendency, may undergo isomerization in two directions:

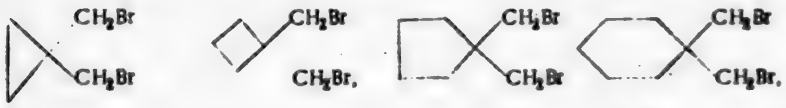


The dihalo derivative of the cyclobutane series formed by the first alternative readily reacts with zinc dust to form methylenecyclobutane, whereas the unsaturated dihalo derivative formed by the second route and containing halogen atoms in positions 1 and 4 will be largely subjected, as follows from Demyanov's researches [16], to reduction to 2-methyl-1-butene and only in small degree to cyclization.

Introduction of iodine ions into the reaction mixture leads to substitution of iodine for one or both of the halogen atoms both in dichlorodimethylcyclopropane and in dibromodimethylcyclopropane. Since the bromine possesses the greater atomic radius, it will facilitate closure of the second cyclopropane ring and thereby lead to increased yields of spiropentane.

At the same time the enhanced tendency of α-iodo derivatives to rupture of the three-membered ring [17] leads to some increase in yields of the open-chain hydrocarbon, 2-methyl-1-butene.

It follows from the above considerations that in the dibromodimethylcyclane series



closure of the three-membered ring will occur most readily in dibromodimethylcyclohexane and with the most difficulty in dibromodimethylcyclopropane. And indeed the formation of spiro-(2,5)-octane takes place in a yield of 91% [18].

In previous communications [19,20] we showed that α-halo derivatives of the cyclopropane series readily isomerize to unsaturated open-chain halo derivatives. This change is quantitative for iodo derivatives, less pronounced for bromo derivatives, and least pronounced for chloro derivatives. It follows from the data of the present investigation that in the case of 1,1-dihalodialkylcyclopropanes one of the directions of the reaction is the enlargement of the cyclopropane ring to the cyclobutane ring. Olefinic compounds are also formed by a mechanism similar to that for the α-halodialkylcyclopropanes.

EXPERIMENTAL

Tetrachloroneopentane [9]: Into a half-liter three-necked flask fitted with a reflux condenser and a stirrer was introduced 140 g PCl_5 and sulfur dioxide was passed through until the crystals disappeared completely. To the resultant mixture of $SOCl_2$ and $POCl_3$ was added 14 g pentaerythritol (0.1 mole); then under good stirring 8 g pyridine was added very slowly from a dropping funnel. With increasing evolution of heat the flask was cooled externally with iced water. The mixture was then gently boiled for 3 hours with stirring. This period sufficed for driving off the SO_2. After cooling, the flask contents were poured into iced water and stirred until the $POCl_3$ had been completely decomposed. The crystalline tetrachloroneopentane settled to the bottom and was collected by decantation or filtration. The product melted at 97° after recrystallization from alcohol, in agreement with the literature. Yield 21 g.

Tetrabromoneopentane was prepared from pentaerythritol and PBr_3 [10].

Tetraiodoneopentane was prepared from tetrabromoneopentane by the action of sodium iodide in methyl-ethyl ketone [10]. The product melted rather lower than stated in the literature.

Dehalogenation of tetrachloroneopentane.

a) In aqueous alcohol. Into a flask were introduced 21 g tetrachloroneopentane, ** ml alcohol, 17.5 ml water, 25 g zinc dust, 10.6 sodium carbonate and 2.5 g sodium iodide. The mixture was boiled. Formation of a hydrocarbon was not observed. The whole of the tetrachloro compound was recovered unchanged.

b) In ethylene glycol. The ratios of the reactants were the same as in a. Instead of aqueous alcohol, anhydrous ethylene glycol was used. Water was not added. The mixture was heated at 180-190°. 3 g of product distilled over. The product was distilled after washing with water and drying. The first drops came over at 40° and possessed a hydrocarbon odor. The main bulk came over at 80° and proved to consist of an unsaturated chloro compound. It was not investigated more closely.

c) In acetamide in presence of sodium carbonate. 21 g tetrachloroneopentane, 90 g anhydrous acetamide, 15 g sodium carbonate and 50 g zinc dust were put into a flask fitted with a stirrer and reflux condenser. The mixture was heated and intensively stirred. The reflux condenser was filled with warm water and connected through its upper end with a good cooling coil. Hydrocarbon began to form at 170-180°. Yield about 40%.

The hydrocarbon was washed with water, dried over calcium chloride and distilled over metallic sodium. The hydrocarbon began to boil at 33° but the main mass came over at 38-42°.

Raman spectrum: 305(2), 354(5), 373(3), 581(1), 613(1/2), 657(2), 779(1), 872(3), 907(2), 957(10), 1033(1), 1150(1/2), 1191(2), 1393(2), 1428(3w), 1654(1/2), 1678(8), 2861(1), 2902(4), 2921(4), 2952(5), 2989(8), 3069(3).

d) In acetamide in presence of sodium carbonate and sodium iodide. The experiment was performed as above. Supplementary addition of 5 g sodium iodide was made to the reaction mixture. Yield of hydrocarbon 45% of theory. B. p. 35-42.5°.

Raman spectrum: 305(2), 354(3), 375(2), 583(1), 613(1), 658(1), 777(1), 872(3), 905(2), 957(10), 1033(3), 1150(1), 1191(1), 1394(3), 1427(4w), 1654(2), 1679(5), 2828(1), 2857(1), 2902(2), 2923(2), 2951(3), 2988(6), 3065(4).

Dehalogenation of tetrabromoneopentane.

a) In aqueous alcohol. Experiments were performed in Gustavson's conditions. The results and the Raman spectroscopic data were presented in a previous paper [13].

b) In acetamide in presence of sodium carbonate. 38 g tetrabromoneopentane, 90 g anhydrous acetamide, 15 g sodium carbonate and 25 g zinc dust were used. The dehalogenation conditions were the same as in previous experiments. Hydrocarbon yield about 40% of theory. B. p. 35-42°.

Raman spectrum: 305(3), 353(2), 371(2), 581(1), 613(1), 657(1), 779(1), 873(3), 907(2), 957(10), 1032(3), 1150(1), 1191(1), 1394(3), 1429(4), 1654(2), 1679(5), 2829(1), 2861(1), 2900(2), 2921(2), 2947(2), 2989(5), 3070(3).

Dehalogenation of tetraiodoneopentane.

a) Zinc dust does not react with tetraiodoneopentane in aqueous alcohol.

b) In acetamide in presence of sodium carbonate and sodium iodide. 54 g tetraiodoneopentane, 90 g anhydrous acetamide, 15 g sodium carbonate, 5 g sodium iodide and 35 g zinc dust were taken. Reaction started at as low as 140-150°. Hydrocarbon yield about 80% of theory. B. p. 38-42°.

Raman spectrum: 305(3), 354(2), 374(2), 581(2), 613(1), 658(2), 777(1), 872(4), 905(2), 957(10), 1033(5), 1191(1), 1395(3), 1428(4 w), 1654(1), 1678(4), 2867(2), 2902(2), 2952(3), 2989(6), 3062(4).

c) In acetamide (without addition of sodium carbonate and iodide.) Conditions and quantities as in b). Reaction occurred at 160°. Yield about 80%. B. p. 36-42°.

Raman spectrum: 305(3), 354(2), 581(2), 613(1), 658(2), 779(4), 872(5), 905(1), 957(10), 1033(5), 1191(1), 1395(4), 1428(5 w), 1654(2–3), 1679(2–3), 2865(2), 2908(2), 2949(3), 2959(6), 3065(4).

SUMMARY

1. Zinc dust reacts with tetrahalc neopentanes in anhydrous acetamide to form a hydrocarbon mixture consisting of methylenecyclobutane, spiropentane afid 2-methyl-1-butene.

2. The spiropentane content of this mixture increases in passage from tetrachloroneopentane to tetraiodoneopentane. Tetrabromoneopentane occupies an intermediate position.

3. Yields of spiropentane from tetraiodoneopentane do not change when sodium carbonate is present; this fact confirms its role as a means for regeneration of the iodine ion.

4. It is suggested that the rising yield of spiropentane in the order tetrachloroneopentane-tetrabromoneopentane-tetraiodoneopentane is related to the magnitude of the atomic radii of the halogens.

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MONOVINYLACETYLENE HOMOLOGS

II. ADDITION OF METHYL ALCOHOL TO Δ_1-CYCLOPENTENYL-ACETYLENE

I. A. Favorskaya and L. V. Fedorova

The present investigation was undertaken with the aim of studying the order of addition of methyl alcohol to the monovinylacetylene hydrocarbon series containing an endocyclic double bond. Particular interest is attached to the product of addition of one molecule of methyl alcohol to Δ_1-cyclopentenylacetylene in the 1,2-position, i.e., at the triple bond. Dienic ethers of the general formula $C_nH_{2n-4}O$, i.e., ethers in which one of the conjugated double bonds is in a five- or six-membered ring, have not previously been investigated. Nevertheless these compounds are of undoubted interest since we can use them, via the diene synthesis, for the preparation of diverse derivatives of bicyclic ketones of the decalone and hexahydroindanone series.

The experimental material relating to the addition to hydrocarbons containing adjacent double and triple bonds concerns mainly their simplest representative – monovinylacetylene. Work with this hydrocarbon has shown that addition may proceed in the 1,4-position or at the triple bond in the 1,2-position. In isolated cases the addition apparently takes place at the double bond.

The study of the order of addition of various reagents to systems containing a double and a triple bond is complicated by a series of secondary reactions which are made possible by the isomerizing tendency of the initially formed products with an allenic structure. Depending on the conditions, the isomerization of allenic compounds may proceed either in the direction of formation of acetylenes or in that of formation of dienes.

Addition of various reagents to monovinylacetylene homologs leads mainly to products of apparent or actual addition at the triple bond.

Addition of HCl to the simplest homolog of vinylacetylene, isopropenylacetylene, was studied by A. E. Favorsky [1]. Addition at the triple bond led to formation of chlorisoprene. Carothers and Coffman [2] obtained the same results when performing the reaction in similar conditions.

Homologs of monovinylacetylene not containing acetylenic hydrogen, of the general formula $CH_2=CH-C\equiv C-R$ (where R = CH_3, C_2H_5 or C_4H_9), react with concentrated hydrochloric acid to give products of addition at the triple bond [3].

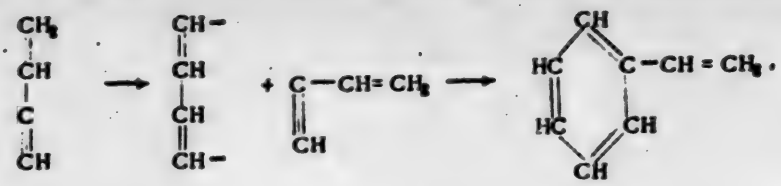
Carothers and Coffman [2] studied the reaction of sec. butenylacetylene and Δ_1-cyclohexenylacetylene with hydrochloric acid. On the analogy of the reaction with vinylacetylene itself, the authors assumed that addition took place at the 1,4-position with formation of the corresponding allenes. The latter undergo subsequent isomerization to diene derivatives, but since no intermediate products with an allenic structure were isolated, the reaction mechanism remained uncertain. Chlorides of similar structure may be obtained by addition of HCl at the triple bond.

A. I. Zakharova [4] studied the action of alcoholic alkali on sec. butenylacetylene; methyl alcohol added on at the triple bond.

The literature contains isolated facts, however, which confirm the susceptibility of vinylacetylene homologs to addition reactions in the 1,4-position. In an investigation of the addition of triphenylmethane to isopropenylacetylene, A. F. Thompson [5] obtained 1,1,1,6,6,6-hexaphenyl-2,3-hexadiene as the sole reaction product. Ozonolysis of the latter yielded triphenylacetic acid and 1,1,1-triphenyl-3-butanone.

Vinylacetylene homologs tend to dimerize in the same way as butadiene (Diels-Alder diene reaction). For the dimerization of vinylacetylene itself Dykstra [6] proposed a mechanism based on intermediate formation of an allenic structure due to addition in the 1,4-position.

According to A. E. Favorsky [7] the dimerization of monovinylacetylene in presence of methyl alcohol may be represented by the following scheme:



A similar mechanism was proposed by A. E. Favorsky and A. I. Zakharova [8] for the dimerization of isopropenylacetylene. It was shown that heating of isopropenylacetylene with methyl alcohol at 120° results in formation of 1-pseudobutenyl-3,4-dimethylbenzene in 50% yield.

Our own observations indicate that dehydration of higher tertiary acetylenic alcohols over unburnt porcelain or $MgSO_4$ leads to formation of hydrocarbon dimers of the styrene type. The same observation was made by Shikhiev [9] on dehydration of methyl-n-propylethinyl carbinol. The yield of the dimer fraction of the hydrocarbon varies within wide limits depending on the structure of the carbinol undergoing dehydration. Thus, for example, in the dehydration of diisopropylethinyl carbinol, the dimer is the main reaction product (approx. 90%), whereas in the dehydration of α, α'-ethinylcyclopentanol a hydrocarbon dimer is not generally formed.

In this investigation of the addition of methyl alcohol to a monovinylacetylenic hydrocarbon containing an endocyclic double bond, the starting material was the Δ_1-cyclopentenylacetylene previously prepared by us.

It has been noted [10] that cyclopentenylacetylene possesses a yellow color which cannot be accounted for by its established structure. In order to clarify this problem, the hydrocarbon was purified via the copper derivative. The hydrocarbon regenerated from the copper derivative was colorless. Nevertheless the constants of the purified, colorless hydrocarbon almost coincided with those of the yellow hydrocarbon. The color was evidently due to the presence of traces of impurities which did not modify the constants.

On plotting the ultraviolet absorption spectra with a SP-22 spectrophotometer, using a cell of variable thickness, it was established that the yellow hydrocarbon has an absorption maximum at a wavelength of λ2800 3645 A. The absorption spectrum of dimethylfulvene contains three fairly strong bands at 2300, 2700 and 3650 A [11]. There are no experimental data in the literature for the spectrum of fulvene itself; however, we may assume that in the present case substitution has no influence on the absorption spectrum since it is known that the electron spectrum in the ultraviolet region is caused by conjugated double bonds.

On the basis, therefore, of the spectroscopic investigation of colored cyclopentenylacetylene, we established that it is contaminated with methylfulvene

The methylfulvene content of the mixture was determined by the oxidation method. It was found that the content of oxalic and acetic acids in the oxidation products only amounts to a few percent. After our paper [10] had gone to press a paper was published by Heilbron [12] which reported the preparation of Δ_1-cyclopentenylacetylene by dehydration of α, α'-ethinylcyclopentanol over aluminum phosphate. According to Heilbron, Δ_1-cyclopentenylacetylene is a faint-yellow liquid with a λ_{max} at 2270 A.

Addition of methyl alcohol to Δ_1-cyclopentenylacetylene was effected by us in presence of BF_3 and HgO.

Hennion and Nieuwland [13] added methyl alcohol to monovinylacetylene in presence of BF_3 and HgO. In these conditions additions of three molecules of methyl alcohol took place with formation of 2,2,4-trimethoxybutane. By analogy with Carother's results [14], the authors propose the following scheme:

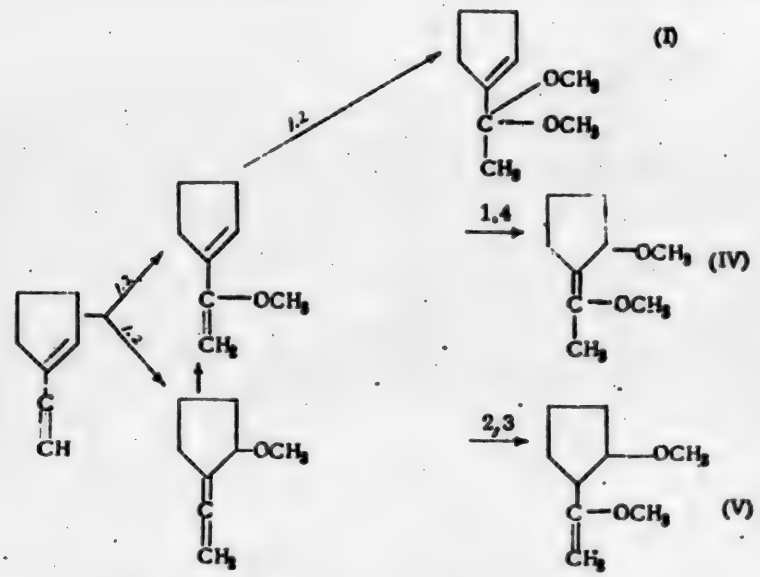
$$CH_2 = CH - C \equiv CH \rightarrow CH_3OCH_2 - CH = C = CH_2 \rightarrow$$

$$\rightarrow CH_3OCH_2 - C \equiv C - CH_3 \rightarrow CH_3OCH_2 - CH_2 - C(OCH_3)_2 - CH_3.$$

Since, however, no intermediate products were isolated the mechanism is still debatable.

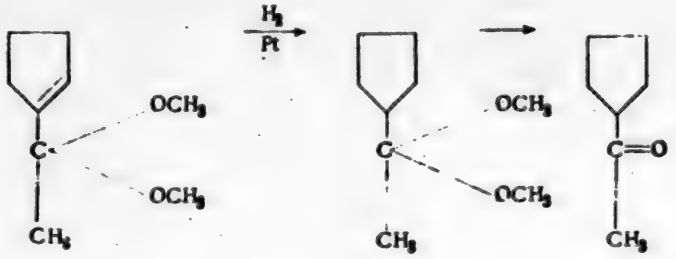
We isolated and characterized the following compounds as a result of reaction in the above-noted conditions of methyl alcohol with Δ_1-cyclopentenylacetylene: 2,2'-dimethoxy-2-Δ_1-cyclopentenylethane (I) -16%; 2,2'-dimethoxy-2-Δ_2-methoxycyclopentylethane (II) - 13 %; and the dimer $C_{16}H_{24}O_2$ (III) -45 %.

Addition of two molecules of methyl alcohol to Δ_1-cyclopentenylacetylene may proceed according to the scheme:



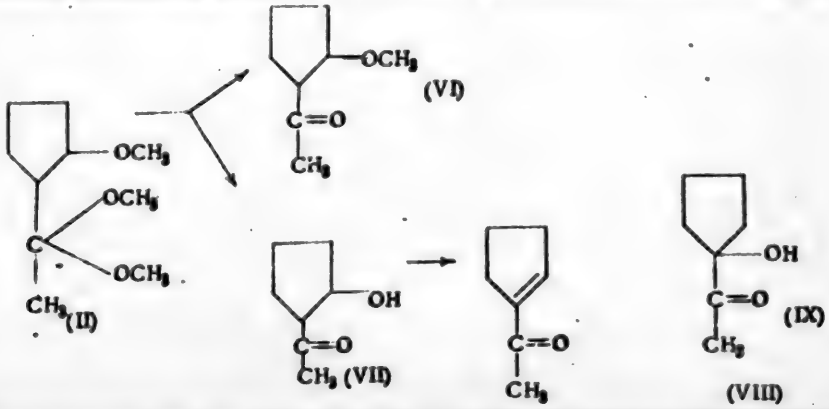
Depending on the order of addition of the alcohol to the hydrocarbon, the dimethoxy derivative of the hydrocarbon may have the structure corresponding to formulas (I), (IV) or (V).

The structure of the product of addition of two molecules of alcohol was established by hydrogenation and by hydrolysis in presence of dilute hydrochloric acid. Hydrolysis of the hydrogenation product yielded methylcyclopentyl ketone.



On the basis of this observation we may say that the product of addition of two molecules of the alcohol to Δ_1-cyclopentenylacetylene has a ketal structure and corresponds to formula (I).

The structure of product (II) was established in the following manner: Hydrolysis in the cold in presence of dilute hydrochloric acid yielded 1-methoxy-2-acetylcyclopentane (VI). Hydrolysis of (II) by heating to 80° in presence of sulfuric acid and mercuric sulfate led to formation of the unsaturated ketone (VIII) [12].

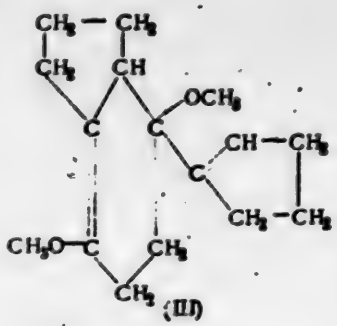


The intermediately formed β-ketoalcohol (VII) is unstable and splits off water to form the unsaturated ketone (VIII).

In these conditions the isomeric α-ketoalcohol, 1-hydroxy-1-acetylcyclopentane (IX) is perfectly stable and does not form the unsaturated ketone.

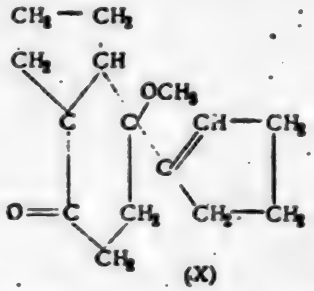
On the basis of these data we may say that the structure of (II) corresponds to 2,2'-dimethoxy-2-Δ_2-methoxy-cyclopentylethane.

Compound (III) is the dimer of the product of addition of one molecule of methyl alcohol to the hydrocarbon. Depending upon the order of addition of the alcohol in the 1,4-position or at the triple bond in the 1,2-position, the structure of the addition product will be either that of an allene ether or a diene ether with conjugated double bonds. It is quite obvious that the structure of dimer (III) will be determined by the structure of the monomeric ether.

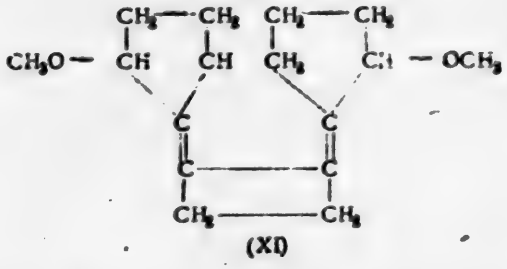


(III)

In the present investigation we did not succeed in isolating compound (III) in the analytically pure form in spite of repeated distillation at 0.1 mm. By hydrolyzing compound (III) in presence of dilute hydrochloric acid we obtained product (X), $C_{15}H_{22}O_2$, which contained only one methoxyl group, did not contain a hydroxyl group, and formed a semicarbazone. On the basis of these facts we attribute the structure 7-methoxy-7-Δ_1-cyclopentenylhexahydroindanone-4 (X) to the product of hydrolysis



(X)



(XI)

A similar ketone may be obtained by hydrolysis of the dimer which contains two nonequivalent methoxyl groups. Consequently the most probable formula for the structure of the dimer is (III) – 7-methoxy-7-Δ_1-cyclopentenyl-5,6,7,8-tetrahydroindane.

The tetrahydroindane (III) is formed by diene condensation of the monomeric diene ether. Compound (III) is not the dimer of the allenic ether (1,4 addition) since ketone (X) cannot be formed by hydrolysis of the dimer of structure (XI).

Hence in our investigation we were unable to isolate the intermediate products which would have confirmed the addition of methyl alcohol to Δ_1-cyclopentenylacetylene in the 1,4-position. The isolated products of the reaction (I and III) can be obtained by direct addition of methyl alcohol to the unsaturated ketal, which addition does not proceed according to the Markovnikov rule.

EXPERIMENTAL

Δ_1-Cyclopentenylacetylene (purified through the copper derivative) is a colorless liquid with the characteristic odor of acetylenic hydrocarbons:

B. p. 57.5-58° at 100 mm; d_4^0 0.8731; d_4^{20} 0.8596; n_D^{20} 1.4391; n_α^{17} 1.48825; n_β^{17} 1.50322; MR_D 30.94; calculated 29.86

0.1235 g substance: 0.4119 g CO_2; 0.0954 g H_2O. Found %: C 90.98; H 8.65. Calculated %: C 91.24; H 8.76.

For the constants of the unpurified methylfulvene-containing hydrocarbon see [10].

Oxidation of yellow, methylfulvene-containing cyclopentenylacetylene. 20 g of hydrocarbon was taken for oxidation, which was effected by the normal method with the calculated amount of potassium permanganate. The oxidation results are set out in Table 1. Oxidation of methylfulvene would be expected to give acetic and oxalic acids, but Table 1 shows that the oxalic acid content of the oxidation products does not exceed 2-3%. The volatile acids contain 96% formic acid; therefore not more than a small percentage of acetic acid could also have been formed. It follows that only a small percentage of methylfulvene is present in the mixture.

Addition of Methyl Alcohol to Cyclopentenylacetylene.

1.5 g red HgO, 0.7 g $BF_3(C_2H_5)$ 20 and 0.5 ml CH_3OH was heated for a few minutes at 50-60°. A small quantity of the alcohol (about 10 ml) was added to the catalyst. The remaining alcohol and the hydrocarbon were slowly added from a dropping funnel. The reaction mass was vigorously stirred. The flask was cooled with water. After the whole of the hydrocarbon had been added, stirring was continued for another few hours. The solution was neutralized with sodium methylate and the alcohol distilled off. Several fractionations gave three main reaction products: 2,2'-dimethoxy-2-Δ_1-cyclopentenylethane (I), 2,2'-dimethoxy-2-Δ_2-methoxycyclopentenylethane (II), and the dimer $C_{13}H_{24}O_2$ (III). The experimental conditions and product yields are detailed in Table 2.

TABLE 1

Amount					Analysis of Ca salt of oxalic acid		
of hydrocarbon oxidized (g)	of normal NaOH for titration of volatile acids (in ml)	of formic acid (%)	of non-volatile acids (%)	of oxalic acid (%)	wt. of Ca salt (g)	wt. of CaO (g)	% Ca found*
20 —	114.3	96.0	14.85	2.7	0.1380 0.1447	0.0525 0.0560	27.1 27.6

TABLE 2

Reaction of Methyl Alcohol with Δ_1-Cyclopentenylacetylene

No.	Amount of reactants		duration of experiments (hours)	temperature	dimethoxy deriv. (I) (in %)	trimethoxy deriv. (II) (in %)	Dimer $C_{13}H_{24}O_2$ (III) (in %)
	hydrocarbon (in g)	methyl alcohol (in g)					
1	24	24	6	20—23°	15.6	13	43.7
2	15	30	6	25—26	15.8	12.4	45

Investigation of the Product of Addition of Two Molecules of Methyl Alcohol to Δ_1-Cyclopentenylacetylene (I)

B. p. 71-72° at 17 mm; d_4^0 0.9638; d_4^{20} 0.9467; n_D^{20} 1.4503; MR_D 44.39; calculated 44.18

0.1066 g substance: 0.2718 g CO_2; 0.0960 g H_2O; 0.1110 g substance; 0.2813 g CH_3; 0.0995 g H_2O; 0.1336 g substance; 19.82 g C_6H_6; Δt 0.211°. Found %: C 69.53, 69.11; H 10.08, 10.03; M 148.2. $C_9H_{16}O_2$. Calculated % C 69.24; H 10.26; M 156.2.

Hydrogenation of the unsaturated ketal (I) was performed in ether solution in presence of platinum black. 4.15 g substance in 30 ml ether with 0.3 g Pt black. The theoretical hydrogen requirement was 594.5 ml, whereas 660 ml was taken up (i.e. 110%). The ether was distilled off from the hydrogenation product, after which 14 ml water and 0.5 ml hydrochloric acid were added to the residue. The mixture was stirred at room temperature for 1.5 hours. The upper layer was removed and the aqueous layer was saturated with potassium carbonate and extracted with ether. The ethereal solution was dried with potassium carbonate. 2.2 g substance was obtained with b. p. 94-95° at 105 mm., n_D^{20} 1.4425; semicarbazone with m. p. 143-145°. These data are in accord with those in the literature for methylcyclopentyl ketone [15].

* $C_2H_4Ca \cdot H_2O$. Calculated %: Ca 27.44.

B. p. 66-67° at 3 mm; n_D^{20} 1.4465; d_4^{0} 0.9999; d_4^{20} 0.9840; MR_D 51.096; calculated 51.109

0.1306 g substance: 0.3062 g CO_2; 0.1225 g H_2O. 0.1028 g substance: 0.2408 g CO_2; 0.0958 g H_2O. 0.1352 g substance; 18.78 g C_6H_6 Δt 0.20°. Found %: C 63.94, 63.88; H 10.49, 10.43; M 186.5. $C_{10}H_{16}O_3$. Calculated %: C 63.83; H 10.65; M 188.36.

Hydrolysis of product (II).

1) 3.5 g substance and 9 ml water with 3-4 drops hydrochloric acid were stirred at room temperature for 1.5 hours. The product was neutralized with potassium carbonate, salted out and dried over calcined K_2CO_3. Substance (VI), 1-methoxy-2-acetylcyclopentane, was obtained with b. p. 131-132° at 140 mm. Yield 2 g.

B. p. 114-115° at 72 mm; $n_D^{19.5}$ 1.4485; d_4^{0} 1.0009; $d_4^{19.5}$ 0.9851; MR_D 38.65; calculated 38.598.

0.0995 g substance: 0.2463 g CO_2; 0.0850 g H_2O. 0.0566 g substance: 0.1403 g CO_2; 0.0503 g H_2O. 0.1330 g substance; 18.92 g C_6H_6; Δt 0.27°. 0.0170 g substance: 7 ml 0.1N $Na_2S_2O_3$. Found %: C 67.54, 67.63; H 9.55, 9.94. M 134.9; OCH_3 21.28. $C_8H_{14}O_2$. Calculated %: C 67.54; H 9.93; M 142.19; OCH_3 21.83.

2) 5 g substance (II) was heated with vigorous stirring on the water bath for 1.5 hours with 25 ml 10% H_2SO_4 and a few crystals of $HgSO_4$. After cooling the reaction mass was neutralized and extracted with ether. The ethereal solution was dried with potassium carbonate. 3.5 g of substance (VIII) was obtained with b. p. 68-70° at 16 mm. Semicarbazone m p 204°. No depression in melting point resulted when mixed with the semicarbazone of 1-acetylcyclopentene-1 obtained by hydration of Δ_1-cyclopentenylacetylene.

Hydration of cyclopentenylacetylene. To a mixture consisting of 0.6 g H_2SO_4, 0.6 g $HgSO_4$ and 45 ml 70% aqueous methyl alcohol was slowly added dropwise 13 g of the hydrocarbon. Addition was effected at such speed that the temperature in the reaction flask did not rise above 50-55°. At the conclusion of the reaction the mixture was poured into a solution of sodium carbonate containing ether. The ethereal solution of the ketone was dried over calcined potassium carbonate. After distilling off the ether and methyl alcohol, the ketone (VIII) was distilled in vacuum. Yield 52.8% of theory.

B. p. 61-61.5° at 12 mm, 54° at 8 mm; n_D^{16} 1.4824; d_4^{0} 0.9712; d_4^{16} 0.9586; MR_D 32.78; calculated 31.87.

0.0936 g substance: 0.2612 g CO_2; 0.0770 g H_2O. 0.1577 g substance: 15.72 g C_6H_6; Δt 0.47°. Found %: C 76.12; H 9.20; M 110.5; $C_7H_{10}O$. Calculated %: C 76.32; H 9.15; M 110.15.

The semicarbazone of 1-acetylcyclopentene-1* was prepared. Its. m. p. after two recrystallizations from alcohol was 206-208°.

0.0934 g substance: 20.6 ml N_2 (771.3 mm, 23°). Found %: N 25.1 $C_8H_{13}ON_3$. Calculated %: N 25.13.

Hydration of α,α'-ethinylcyclopentanol. To a mixture of 0.6 g H_2SO_4, 0.6 g $HgSO_4$ and 45 g 70% aqueous methanol was added 15 g of the carbinol. The mixture was heated to 70° and stirred for 2 hours. The reaction products were worked up as in the case of hydration of α-α'-cyclopentenylacetylene. 12.5 g α-ketoalcohol (IX) was obtained (yield 71%).

B. p 73-73.5° at 8 mm; n_D^{16} 1.4645; n_D^{20} 1.4642; d_4^{0} 1.0487; d_4^{20} 1.0323; MR_D 33.83; calculated 33.86.

0.1527 g substance: 0.3666 g CO_2, 0.1250 g H_2O. 0.2636 g substance; 15.66 g C_6H_6; Δt 0.71°. 0.0902 g substance: 15.66 g C_6H_6; Δt 0.24°. Found %: C 65.46; H 9.16; M 132, 124. $C_7H_{12}O_2$. Calculated %: C65.59; H 9.43; M 128.12.

The semicarbazone was prepared and melted at 174-175° after recrystallization from alcohol.

Investigation of Dimer (III)

B. p. 138-140° at 1.5 mm; n_D^{23} 1.5150.

0.1198 g substance: 0.3335 g CO_2; 0.1028 g H_2O. 0.0855 g substance: 0.2378 g CO_2; 0.0756 g H_2O. 0.1575 g substance: 16.51 g C_6H_6; Δt 0.19°. 0.1914 g substance: 16.63 g C_6H_6; Δt 0.24°. 0.0236 g substance: 10.6 ml 0.1 . $Na_2S_2O_3$. Found %: C 75.92, 75.85; H 9.60, 9.89; M 260, 248.4; OCH_3 23.20; $C_{16}H_{24}O_2$. Calculated %: C 77.37; H 9.7; M 248.3; OCH_3 25.0

* 1-Acetylcyclopentene-1 was prepared [12] by boiling Δ_1-cyclopentenylacetylene with 90% formic acid. The constants of the ketone deviate slightly from our data.

Hydrolysis of the dimer. 3.5 g dimer was energetically stirred at room temperature with 25 ml ethyl alcohol, 8 ml water and 1.5 ml HCl for 3 hours. The mixture was salted out with potassium carbonate, extracted with ether and dried with K_2CO_3. 2.2 g of product (X) was obtained with b. p. 130-134° at 1 mm; b. p. 94-96° at 0.1 mm. n_D^{22} 1.5190.

0.0784 g substance: 0.2197 g CO_2; 0.0659 g H_2O. 0.0749 g substance: 0.2103 g CO_2; 0.0631 g H_2O. 0.1325 g substance: 18.84 g C_6H_6 Δt 0.16°. 0.0190 g substance: 4.1 ml 0.1 $Na_2S_2O_3$. 0.0246 g substance: 5.7 ml 0.1 N $Na_2S_2O_3$. Found %: C 76.51, 76.57; H 9.42, 9.43; M 227.8; OCH_3 11.15, 11.16. $C_{15}H_{22}O_2$. Calculated %: C 76.89; H 9.46; M 234; OCH_3 13.25.

The semicarbazone was prepared and recrystallized from alcohol; m. p. 230-235° with decomposition. Test for hydroxyl groups was negative.

SUMMARY

1. Methyl alcohol reacts with Δ_1-cyclopentenylacetylene in presence of boron trifluoride and mercuric oxide with simultaneous addition of one, two and three molecules of the alcohol.

2. The product of addition of one molecule of the alcohol is converted in the reaction conditions into the dimer $C_{16}H_{24}O_2$, which on hydrolysis in an acid medium is transformed in turn into a ketone – 7-methoxy-7-Δ_1-cyclopentenylhexahydroindanone-4.

3. Addition of two molecules of methyl- alcohol to Δ_1-cyclopentenylacetylene takes place at the triple bond with the formation of an unsaturated ketal.

4. The product of addition of three molecules of methyl alcohol to the hydrocarbon corresponds in structure to 2,2'-dimethoxy-2-Δ_2-methoxycyclopentylethane.

5. It is shown that the yellow color of Δ_1-cyclopentenylacetylene is due to a trace of methylfulvene.

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* See Consultants Bureau translation, p. 701.

DECOMPOSITION OF BENZOYL PEROXIDE IN A MEDIUM OF SOME VINYL COMPOUNDS

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Investigation of the decomposition of benzoyl peroxide in a medium of vinyl compounds has great practical and theoretical interest [1-6]. In the study of polymerization processes great interest attaches to clarification of the role of peroxides and to the character of their decomposition during reaction with vinyl compounds. As we know [7], benzoyl peroxide and hydrogen peroxide sometimes decompose according to the scheme:

$$(C_6H_5CO)_2O_2 \rightarrow (C_6H_5CO)_2O + O;$$

$$H_2O_2 \rightarrow H_2O + O.$$

It is also known [8] that benzoyl peroxide decomposes according to the following schemes when heated or exposed to light rays:

$$(C_6H_5CO)_2O_2 \rightarrow C_6H_5 - C_6H_5 + 2CO_2;$$

$$(C_6H_5CO)_2O_2 \rightarrow C_6H_5 - COO - C_6H_5 + CO_2.$$

The decomposition of benzoyl peroxide is much more complicated in various solvents. In this case free radicals are formed:

$$(C_6H_5CO)_2O_2 \rightarrow C_6H_5 + C_6H_5COO' + CO_2,$$

$$C_6H_5COO' \rightarrow C_6H_5' + CO_2.$$

A series of products may be formed as a result of reaction of the free radicals with the solvent [9-11]:

$$C_6H_5' + C_6H_5Cl \rightarrow C_6H_5 - C_6H_4Cl + H';$$

$$C_6H_5' + ROH \rightarrow C_6H_5 - H + RO'$$

$$\text{or } C_6H_5' + H';$$

$$C_6H_5COO' + C_6H_5Cl \rightarrow C_6H_5COOH + C_6H_4Cl'.$$

According to the literature, therefore, the decomposition of benzoyl peroxide may proceed either with release of oxygen [12-15] or with formation of free radicals, e.g., phenyl and benzoate radicals [16-19].

In the course of a study of polymerization processes it was important to establish the possibility of breakdown of peroxides by a mechanism involving oxidation. Bearing in mind that the literature [9] does not consider all the conditions, in particular, of polymerization processes, we decided that a closer investigation of the mechanism of decomposition of peroxides in a series of reactions was necessary.

The induction process proceeds through formation of intermediate peroxy compounds. The proposals of Gelissen and Hermans [10] and of a number of other workers [20 21] on the course of decomposition of benzoyl peroxide apply only in presence of saturated and inert solvents and are directly related to the polymerization reaction.

The present authors have studied the decomposition of benzoyl peroxide in a medium of vinyl acetate methyl methacrylate, styrene and vinyl ethers. Peroxides were used both in small and relatively large amounts in order to effect a more detailed investigation of the decomposition products. The purpose of introduction of large amounts of benzoyl peroxide into the process was to isolate the products which form free radicals during conversion and dimerization. The very first experiments showed that in presence of a large excess of benzoyl peroxide, the polymerization reaction starts remarkably quickly and leads to formation of a polymer enclosing particles of peroxide. In order to avoid this behavior, an inert solvent (petroleum ether) was utilized. The solvent appreciably reduced the speed of polymerization, which permitted degrees of decomposition of benzoyl peroxide of up to

90% to be attained. These conditions fully permitted the investigation of peroxide-breakdown products. In Table 1 are presented the results of a study of the process of decomposition of benzoyl peroxide in a series of vinyl compounds.

TABLE 1

Products of Decomposition of Benzoyl Peroxide in Vinyl Compounds

No.	Used in reaction			Obtained in the reaction			Volume of O_2 obtained (ml)	% decomposition of peroxide with O_2 formation
	$(C_6H_5CO)_2O_2$ (g)	Compound	Weight (g)	O_2	CO_2	H_2O		
1	12.0	$CH_2=CHOCOCH_3$	72.1	0.7480	0.0384	0.0366	523.5	94.33
2	12.0	$CH_2=C(CH_3)COOCH_3$	100.1	0.4043	0.0171	0.0542	282.94	51.0
3	12.0	$C_6H_5CH=CH_2$	104.1	–	0.0738	–	–	–

In these experiments (as well as in others) crystalline and gaseous products formed during benzoyl peroxide decomposition were isolated.

One of these products was benzoic acid. This provides conclusive evidence of symmetrical decomposition according to the scheme: $(C_6H_5CO)_2O_2 \rightarrow 2C_6H_5COO$. Diphenyl and phenyl benzoate were not detected among the reaction products.

EXPERIMENTAL

(Experimental data of V. P. Shishkova)

Decomposition of benzoyl peroxide in a medium of vinyl acetate. The main part of the apparatus for study of decomposition of benzoyl peroxide is a three-necked flask of 800 ml capacity. The central neck is connected to a reflux condenser. One of the other openings serves for a thermometer and the other for insertion of a tube through which nitrogen is bubbled. The nitrogen from a gasholder contains 0.5% oxygen and is passed through a system of Drechsler and Liebig bulbs for absorption of the oxygen, carbon dioxide and water. Directly attached to the reductor are two bottles filled with alkaline pyrogallol solution for absorption of the oxygen. The nitrogen then flows through sulfuric acid, two towers containing soda lime and one tower containing $CaCl_2$, and then through a cotton wool filter. In front of the reaction flask is a three-way piece with one limb connected to a mercury manometer for regulating the gas pressure in the system. From the cotton wool filter the nitrogen (now pure and dry) passes into the reaction flask via a bubbler.

The top of the reflux condenser is connected to a system of absorption vessels in the following order (of gas flow): A buffer vessel to receive any reaction mass or condensate ejected through the reflux condenser, a U-tube containing $CaCl_2$ for absorption of H_2O, two coil-shaped traps cooled to −45 degrees with solid carbon dioxide and acetone, an Ivitsky-type bottle containing aqueous $Ca(OH)_2$, a U-tube containing active carbon for absorption of traces of organic matter not retained in the cooled traps, two U-tubes containing soda lime for absorbing CO_2.

All of the gases evolved in the reaction are driven out with nitrogen and pass through the absorption system before being collected in a gasholder over a saturated aqueous solution of sodium chloride. The amount of oxygen was determined by absorption with alkaline pyrogallol in a "TI-4" apparatus.

Substances used in reactions had the following constants: 1) Vinyl acetate, b. p. 71.5-71.9° (737.4 mm); n_D^{20} 1.3960; 2) petroleum ether, b. p. 80-107°; n_D^{20} 1.4139; 3) benzoyl peroxide, prepared by two recrystallizations from absolute diethyl ether, m. p. 102.7-103.0°.

Into the reaction flask of the above-described apparatus were introduced 72.12 g vinyl acetate, 12.0 g benzoyl peroxide and 120.03 g petroleum ether. The system was filled with pure, dry nitrogen. The temperature of the reaction medium was gradually raised to 86°. The maximum temperature during an experiment was 87.5°. At the end of the first hour, at a temperature of about 53°, the whole of the benzoyl peroxide had dissolved and evolution of fine gas bubbles which rose up was observed. At 70° the mass was observed to boil and condensate at times filled part of the lower bulb of the reflux condenser. The temperature was maintained for 3 hours at 70-86°, after which the reaction flask was cooled while a nitrogen stream was continuously passed through the system. The pressure during an experiment was 18-20 mm. The total duration of an experiment was 5 hours. During a reaction 5000 ml gas containing 10.47 vol % oxygen was collected in the gasholder, the amount being converted to normal temperature and pressure (Table 2).

Thus 94.3% (11.32 g) of the benzoyl peroxide introduced was decomposed with evolution of oxygen. Assuming that CO_2 also originated from decomposition of peroxide, we must assume that 1.76% of the original benzoyl peroxide decomposed to give CO_2.

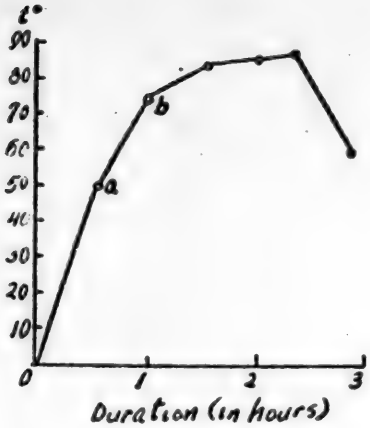
TABLE 2

Taken	g	Obtained	g
CH_2=CHOCOCH$_3$	72.12	Solution of polymer in petroleum ether	107.87
$(C_6H_5CO)_2O_2$	12.00	Crude polymer	91.62
Petroleum ether	120.03	CO_2	0.0384
Total	204.15	O_2	0.7480
		Condensate in trap	1.90
		H_2O	0.0366
		Tube containing active carbon	0.1676
		Total	202.3806

A second possible source of the CO_2 is oxidative decomposition of the starting substances, principally vinyl acetate. This possibility is supported by the fact that the following amount of water was formed during the reaction: a) found 0.0366 g; b) calculated from the CO_2 assuming complete oxidation to H_2O and CO_2, 0.012 g, i.e., the water found was three times as much as would correspond to the amount of CO_2 found whose absorption cannot be quantitiative due to the high velocity of the nitrogen stream.•

In addition to the gaseous reaction products great interest attaches to the products formed directly in the reaction flask. The reaction yielded a polymer which settled out in the form of a viscous, resinous mass, and an upper layer comprising a solution of individual reaction products in petroleum ether. The total quantity of reaction mixture was 199.49 g, from which were isolated 91.62 g "crude polymer" and 107.87 g solution with a marked odor of petroleum ether and a faint odor of vinyl acetate.

The "crude polymer" was dissolved in acetone by heating on the water bath and was treated with 71.5 ml 5% aqueous KOH. A polymer was thus obtained in the form of a white, curd-like mass, and the aqueous acetone alkaline solution containing potassium benzoate was separated. The acid was isolated by treating the residue after evaporation with H_2SO_4 and repeatedly crystallizing it from water. Benzoic acid was identified by the m. p. of 121.5° and by the m.p. of 120.8° of the mixed sample.



From the petroleum ether solution after supplementary freezing at −50° was isolated a further 2.4 g polyvinyl acetate; after this the total solution (101.3 g with n_D^{20} 1.4151) was fractionated to give the following fractions: 1) b. p. 76-85.8° 17.37 g, n_D^{20} 1.4128; 2) b.p. 85.8-102.5°, 77.62 g, n_D^{20} 1.4120; 3) flask residue 4.43 g.

The second fraction was refractionated: 1) b. p. 77-85.5° 9.81 g, n_D^{20} 1.4158; 2) b. p. 85.5-94° 62.36 g, n_D^{20} 1.4135; 3) flask residue 2.90 g, n_D^{20} 1.4154.

The residues from both fractionations were combined and refractionated: 1) b. p. 50-93° 3.91 g; 2) b. p. 50-70° (11 mm) 0.33 g; 3) residue 2.60 g.

The first fraction (3.91 g) obtained by fractionation of the residues was again fractionated: 1) b. p. 65-85° 0.68 g, n_D^{20} 1.4084; 2) b. p. 85-102° 2.55 g, n_D^{20} 1.4138; 3) residue 0.26 g, n_D^{20} 1.4140.

The first fraction had a sharp odor of acetic acid.

On fractionation of the products of reaction contained in the petroleum ether solution, in all the experiments white crystals of benzoic acid were deposited on the sides of the dephlegmator and the condenser (m. p. 121.5°).

Finally, the condensate in the CO_2-cooled trap was examined. In all 1.90 g of readily volatile liquid with a pungent odor was collected. It dissolved completely in water. The aqueous solution gave the character-

• The trap containing $Ca(OH)_2$ solution showed that carbon dioxide begins to come off immediately after solution of the whole of the benzoyl peroxide.

istic reaction for acetaldehyde with fuchsine sulfuric acid.

0.0786, 0.0613 g substance: 0.0035, 0.0030 g CH_3CHO (according to Ripper). Found %: CH_3CHO 4.45, 4.89

II. Decomposition of benzoyl peroxide in methyl methacrylate. Materials used: 1) methyl methacrylate, b. p. 24-31.5° (35-37 mm), n_D^{20} 1.4156; 2) petroleum ether, b. p. 80-107°, n_D^{20} 1.4139; 3) benzoyl peroxide, m. p. 102.7-103.0°.

The experiment was performed in the above-described apparatus but omitting the $Ca(OH)_2$ bottle. Into the reaction flask were charged 100.1 g methyl methacrylate, 120.1 g petroleum ether and 12.0 g benzoyl peroxide. The rate of heating of the reaction mixture is plotted in the diagram. The whole of the benzoyl peroxide had dissolved in about 40 minutes after the start of the reaction at a temperature of about 53°; gas bubbles appeared at the surface of the liquid which rapidly began to grow turbid. A white flocculent precipitate of polymethyl methacrylate settled to the bottom of the reactor; after 1.5 hours the solution was highly viscous and a solid mass of polymer was at the bottom. The total duration of the experiment was 2 hours 40 minutes; the maximum temperature during the experiment was 88°. A total of 5098 ml of gases was collected in the gasholder and the oxygen content was 5.55 vol.%. In the trap, cooled in a Dewar flask, was collected about 2 g substance with a sharp aldehydic odor, n_D^{20} 1.3940 (Table 3).

TABLE 3

Taken	g	Obtained	g
$CH_2=C(CH_3)-COOCH_3$	100.12	Solution	70.33
$(C_6H_5CO)_2O_2$	12.00	Polymer (crude)	157.27
Petroleum ether	120.07	CO_2	0.0171
		Tube containing active carbon	0.0567
Total	232.19	O_2	0.4043
		H_2O	0.0542
		Condensate in trap	1.97
		Total	230.1023

51% (6.1204 g) of the benzoyl peroxide used in the reaction was decomposed to oxygen but if we assume that the CO_2 originated from decomposition of peroxide then the amount of CO_2 found corresponds to 0.78% benzoyl peroxide. The amounts of water found and calculated (on the basis of the CO_2) are in close agreement: Found: 0.054 g, calculated from the CO_2: 0.056 g.

TABLE 4

Taken	g	Obtained	g
$C_6H_5CH=CH_2$	104.14	Solution	232.80
$(C_6H_5CO)_2O_2$	12.0	Condensate	0.92
Petroleum ether	120.0	CO_2	0.0738
Total	236.14	Total	233.79

The upper layer was poured off from the polymer in the flask and cooled to −15° when 1.25 g white crystals came down. M.p. 100.5°; no depression of melting point when mixed with benzoyl peroxide.

III. Decomposition of benzoyl peroxide in a styrene medium. Materials used in the reaction were 104.14 g distilled pure styrene, b.p. 34-35° [10], n_D^{20} 1.5462; 120.0 g petroleum ether and 12.0 g benzoyl peroxide. Duration of experiment 2 hours 17 minutes; maximum temperature 86.5°; total gas volume 3728 ml.

No oxygen was found on analysis of the collected gases. The absence of oxygen is fully understandable when we take into account the ease of oxidation of styrene [22].

The following observations were made in the reaction: 1) The weight of the tube with active carbon increased by 0.0028 g; 2) the amount of condensate in the trap was 0.92 g, n_D^{20} 1.3880; 3) tube containing soda lime increased in weight by a) 0.0552 g, b) 0.0186 g.

In addition a solution of turbid, oily liquid was obtained with a predominant odor of petroleum ether. The weight of the solution was 232.80 g; n_D^{20} 1.4789. On standing the solution deposited a heavy, oily liquid in quantity of 1.9 g; n_D^{20} 1.3485 (Table 4).

On converting the quantity of evolved CO_2 to benzoyl peroxide we obtain a value of 3.38% for decomposition of the peroxide.

IV. Investigation of the reaction of vinyl-n-butyl ether with benzoyl peroxide. (Experimental work by E. P. Gracheva). 100 g vinylbutyl ether and 12 g benzoyl peroxide were placed in a round-bottomed flask fitted with a mechanical stirrer.

After heating for 38 hours the reaction mixture was fractionated: 1) b.p. 94° 97.7 g, n_D^{20} 1.4023, i.e. unchanged vinylbutyl ether; 2) b.p. 74-75° (12 mm) 4.7 g, n_D^{20} 1.4040, d_4^{20} 0.8260.

13.01 mg substance: 14.60 mg H_2O; 32.30 mg CO_2. 10.22 mg substance: 11.61 mg H_2O; 25.43 mg CO_2. Found %: C 67.75, 67.90; H 12.55, 12.71. $C_{18}H_{36}O_3$. Calculated %: C 68.4; H 12.9.

After taking off the above fractions the residue in the flask was a viscous mass (13.1 g). A part of the residue was treated with hot water, filtered from insoluble material and left to stand; large white crystals came down with m.p. 120-121°. Yield 3.75 g. A mixture with benzoic acid did not depress the melting point.

The residue on the filter was insoluble benzoyl peroxide (m.p. 102-103°) in amount of 4.21 g. The other portion of the residue (2.5 g) dissolved in benzene. The solution was saturated with dry ammonia; a voluminous precipitate was formed which was again filtered and subjected to a supplementary extraction with hot benzene. This treatment left a residue of 1.1 g ammonium benzoate on the filter; m.p. 180-181°. It did not depress the melting point of an authentic specimen.

SUMMARY

1. It is shown that in a medium of vinyl compounds benzoyl peroxide is mainly decomposed into benzoic acid and oxygen.

2. The $C_6H_5COO^{\cdot}$ or $CH_3COO^{\cdot}$ radicals may undergo secondary decomposition with loss of oxygen [13].

3. Peroxides are sources of both free radicals and oxygen, and the latter is a catalytic initiator of the free-radical chain reaction of polymerization.

4. Decomposition of benzoyl peroxide in a medium of a series of solvents with formation of free phenyl radicals and benzoate, as established by Gelissen and Hermans, cannot be regarded as the invariable type of reaction in all forms and conditions of processes of polymerization initiated by peroxide.

5. The scheme advanced by us for decomposition of peroxides is fully consistent with the polymerization conditions caused not only by radicals but also by atmospheric oxygen and is in complete accord with the mechanism of action of inhibitors.

6. Benzoyl peroxide does not promote the processes of polymerization of vinyl ethers, which fact is indirect proof of the correctness of our scheme for the decomposition of peroxides. This conclusion is fully consistent with the fact that oxygen does not promote the polymerization of vinylalkyl ethers.

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• See Consultants Bureau translation, p. 541.

ACETYLENIC ALCOHOLS AND GLYCOLS

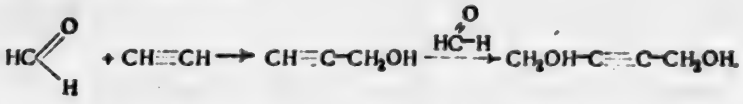
I. SYNTHESIS AND TRANSFORMATIONS OF 1,4-BUTYNEDIOL

M. F. Shostakovsky and A. V. Bogdanova

1,4-Butynediol is prepared by condensation of acetylene with formaldehyde [1,2]. Concerning the transformations of 1,4-butynediol we know that it can be brominated, forms a dimethyl ether [3], and adds on water [4] and hydrogen [5]. Diacetylene can be obtained by chlorination of butynediol followed by detachment of hydrogen chloride [6]. There are indications that pyrroles can be prepared from butynediol. Like acetylene, butynediol can be cyclized, forming hexamethylol benzene which can be oxidized to mellitic acid.

It appeared of interest to us to investigate the reaction of butynediol with vinyl ethers. Such an investigation was also expedient because the only compounds of butynediol containing ethereal groups mentioned in the literature are the dialkyl ethers (dialkoxybutynes). These are prepared by the action of chloromethylalkyl ethers on acetylene dimagnesium bromides [7].

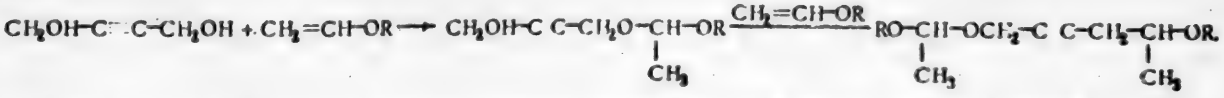
Butynediol is synthesized from formaldehyde and acetylene under the influence of acetylides of metals according to the equation:



A study was made of the effect of temperature, pressure, duration of heating and type of catalyst on the course of this synthesis. We deviated from the literature procedure by not diluting the acetylene with nitrogen, thereby considerably simplifying the experimental technique and increasing the efficiency of the conversion.

With the aim of standardizing the preparative method we performed the synthesis of butynediol by the above-mentioned condensation [2] in an autoclave. Utilization of a catalyst supported on silica gel permits the yield of butynediol to be increased. One portion of catalyst can serve for ten consecutive charges of formaldehyde.

A study was made of the reactions of butynediol with vinylethyl and vinylbutyl ethers according to the scheme:



This reaction was carried out both with a catalyst (traces of acid) and thermally without a catalyst [8].

The reaction yielded mono- and di-α-alkoxyethyl ethers of butynediol in the form of colorless, pleasant-smelling liquids soluble in organic solvents (the monoethers were difficultly soluble in benzene). All the investigated ethers decomposed when heated. Diethylacetal was isolated from the products of decomposition of the di-α-ethoxyethyl ether of butynediol. The di-α-ethoxy ethers were more stable than the corresponding di-α-butoxy ethers and they can be distilled at atmospheric pressure with only partial decomposition. The residues after fractionation of the α-alkoxyethyl ethers of butynediol are transparent, brown resins which decompose explosively when heated. The structure of the mono- and di-α-alkoxyethyl ethers of butynediol was established by hydrolysis [9]. We demonstrated the presence of a triple bond in the derived acetals by hydrogenating the di-α-butoxyethyl ether of butynediol over platinum oxide; the triple bond underwent exhaustive hydrogenation and the acetal was degraded.

Laboratory assistant M. S. Egorova participated in the experimental work.

EXPERIMENTAL

Preparation of 1 4-butynediol. Commercial 30% formalin and technical acetylene were utilized for the synthesis. Commercial reagents of the normal degree of purity were used in preparation of the catalyst.

The catalyst and 217 g formalin were charged into a 2.5 liter rotating autoclave equipped with a thermocouple. A stream of acetylene was passed through the autoclave to establish an acetylene pressure of 13-15 atm. The autoclave was rotated and heated to 97-105° in the course of one hour. After cooling and further addition of acetylene, heating was effected for another 3 hours. During this period 43-49 liters of acetylene was absorbed. After cooling, the autoclave was discharged, the liquid product being carefully decanted from the catalyst. 217 g formalin was added to the catalyst residue in the autoclave and the operation was repeated in the above manner. The discharged product was filtered through filter paper (220 ml filtrate); it consisted of a transparent, yellow liquid. The water was distilled off at 47-50 mm; the residue contained 69.5 g crystalline butynediol, m.p. 55-57°. Yield of technical product 80.8% of theory. Vacuum fractionation of 69.5 g of technical product gave 58.7 g with b.p. 151-152° at 23 mm and a residue of 9.1 g. The latter was a dark-colored resin soluble in water.

The prepared butynediol had b.p. 151-152° at 23 mm; 137-138° at 10 mm; m.p. 57-58°.

Literature data: b.p. 132-135° (5 mm); m.p. 55-58° [2].

15.14 mg substance: 30.85 mg CO_2; 9.41 mg H_2O. 15.47 mg substance: 31.53 mg CO_2; 9.84 mg H_2O. Found %: C 55.61, 55.62; H 6.95, 7.11. $C_4H_6O_2$. Calculated %: C 55.81; H 6.98.

The yield of pure butynediol was 68.3% of the theoretical.

Reaction of butynediol with vinyl ethers. Butynediol with b.p. 137-138° (10 mm) and m.p. 57-58° was used in all the transformations. The butynediol was stored in a bottle from which the air was evacuated. The stopper of this bottle was provided with a tap for creating a vacuum or for filling with nitrogen when a quantity was being weighed out. The vinyl ethers were purified [10] and their constants agreed with those in the literature. Vinylbutyl ether: b.p. 93.5-94°, n_D^{20} 1.4015; vinylethyl ether. b.p. 35.5-36°, n_D^{20} 1.3780.

The dioxane used was purified [11] and had b.p. 101-101.5°; freezing point 11.6°.

a) Catalytic reaction of butynediol with vinylethyl ether in dioxane solution. A solution of 43 g (0.5 mole) butynediol in 50 g dioxane, prepared at +40°, was placed in a three-necked flask fitted with thermometer, stirrer, dropping funnel and reflux condenser. A drop of concentrated hydrochloric acid was added while stirring, and addition was then made dropwise over a period of 3 hours of 75 g vinylethyl ether. During this stage the temperature of the reaction mixture was raised to 36-42°. Addition of the whole quantity of vinylethyl ether was followed by continued heating on the water bath at 48-50° for $2\frac{1}{2}$ hours. The discharged product, a slightly colored liquid, was treated with powdered potassium carbonate and left over the latter overnight. It was filtered, 46.8 g dioxane was distilled off (in a stream of dry nitrogen and in presence of a small crystal of pyrogallol), and the residue distilled in vacuum. The first fraction (14 g) had b.p. 30-134° at 12 mm; the second fraction (89.2 g) had b.p. 134-138° at 12 mm; the third fraction (5.7 g) had b.p. 138-150° at 12 mm. The residue weighed 7.5 g. No condensate was found in the coil of the receiver which was cooled to −40°.

The first fraction was fractionated to remove the dioxane and then combined with the second fraction. Fractional vacuum distillation of the latter gave 88 g of material with the constants: b.p. 126-127° at 8 mm; 254-255° at 736 mm (with slight decomposition); n_D^{25} 1.4400, d_4^{20} 0.9749; MR_D 62.26; calculated 62.19.

0.2572 g substance: 15.81 g benzene: Δt 0.370°. 0.2338 g substance: 15.81 g benzene: Δt 0.340°. Found: M 225.1, 222.7. $C_{12}H_{22}O_4$. Calculated: M 230.29. 3.830 mg substance: 8.804 mg CO_2; 3.300 mg H_2O. 3.604 mg substance: 8.310 mg CO_2; 3.069 mg H_2O. Found %: C 62.72, 62.92; H 9.63, 9.52. $C_{12}H_{22}O_4$. Calculated %: C 62.57; H 9.63.

The isolated product is the di-α-ethoxyethyl ether of butynediol. Yield 76.5%.

b) Reaction of butynediol with vinylethyl ether in the autoclave without catalyst. 43 g butynediol and 75 g vinylethyl ether were introduced into a 0.5 liter autoclave. While rotating, the autoclave was heated to 88-96° in the course of 9 hours. After cooling, 112 g of clear liquid product was discharged and fractionated in vacuum: First fraction b.p. up to 129° at 28 mm −10.5 g; second fraction b.p. 129-131° at 28 mm −90.5 g; third fraction, b.p. 131-134° at 29 mm −2.0 g, residue 4.0 g. In the coil of the receiver, cooled to −40°, 1.0 g of condensate collected.

The first fraction was freed from low-boiling constituents by fractionation and then combined with the second fraction. The low-boiling portion of the first fraction was combined with the condensate in the receiver coil.

The second fraction was the di-α-ethoxyethyl ether of butynediol which had the following constants after fractionation: b.p. 128.0-129.0 at 9.5 mm; n_D^{20} 1.4400; d_4^{20} 0.9752. Yield 78.8% of theory.

Examination of the condensate in the coil of the receiver (cooled to −40°). The condensate contained traces of acetaldehyde (reaction with fuchsin-sulfurous acid). The condensate from this experiment was combined with the condensates from several similar experiments; repeated fractionation at atmospheric pressure then led to the isolation of diethylacetal with the constants: b.p. 102-103.5° (747 mm); n_D^{20} 1.3816; d_4^{20} 0.8295; MR_D 33.12; calculated 33.19.

Isolation of the diethylacetal in this case raises the question of the thermal decomposition of the prepared ethers of butynediol.

c) Preparation of the mono-α-ethoxyethyl ether of butynediol. In the conditions of the above-described experiment 43 g (0.5 mole) butynediol and 37 g (0.5 mole) vinylethyl ether were charged into the autoclave. The rotating autoclave was heated to 81-88° in the course of 1½ hours. After cooling, the clear product (74.5 g) was fractionated in vacuum: First fraction, b.p. 105-128° at 13 mm −9.8 g; second fraction, b.p. 128-129° at 13 mm −30.6 g; residue 29.4 g.

When the residue was cooled it deposited crystals of unchanged butynediol. These were separated from the liquid and weighed 18.9 g after washing with ether and drying in a vacuum desiccator. M.p. 56-57°. The coil of the receiver, cooled to −40°, was found to contain 4.0 g condensate.

The first fraction was divided between the coil condensate and the second fraction. After fractionation the second fraction had the following constants: b.p. 124-124.5° at 10 mm; n_D^{20} 1.4550; d_4^{20} 1.0192; MR_D 41.95; calculated 42.12.

3.580 mg substance: 8.019 mg CO_2; 2.820 mg H_2O. 3.355 mg substance: 7.510 mg CO_2; 2.700 mg H_2O. Found % C 61.13, 61.09; H 8.81, 9.00. $C_8H_{14}O_3$. Calculated %: C 60.73; H 8.92.

The obtained data enable us to identify the product as the mono-α-ethoxyethyl ether of butynediol. Yield 69.1% of theory, calculated on the reacted butynediol.

d) Catalytic reaction of butynediol with vinylbutyl ether in dioxane solution. In the previously described conditions dropwise addition was made, with stirring, of 110 g vinylbutyl ether over a period of 1½ hours to a solution of 43 g butynediol in 50 g dioxane in presence of a drop of concentrated hydrochloric acid. The mixture was then heated to 40° in the course of 3 hours, and after cooling it was treated with potassium carbonate. 48 g dioxane was distilled off in a dry nitrogen stream. The residue was distilled in vacuum: First fraction, 40-117° at 15 mm −18.6 g; second fraction, 117-167° at 12 mm −5.0 g; third fraction, 167-170° at 12 mm −86.8 g; residue 18.6 g. 5 g liquid product collected in the coil receiver which was cooled to −40°.

From the first fraction was isolated 14 g dibutylacetal with b.p. 184.5-185°; n_D^{20} 1.4090; d_4^{20} 0.8280. These constants agree with the literature data [12,13].

Vacuum fractionation of the second and third fractions yielded 90.0 g of a product with the constants: b.p. 152-153° at 3 mm; n_D^{20} 1.4445; d_4^{20} 0.9355; MR_D 81.32; calculated 80.66.

0.2524 g substance: 13.09 g benzene: Δt 0.36°. 0.2394 g substance, 13.09 g benzene: Δt 0.34°. Found: M 274.25, 275.40. $C_{16}H_{30}O_4$. Calculated: M 286.40. 4.230 mg substance: 10.414 mg CO_2; 4.110 mg H_2O. 3.689 mg substance: 9.084 mg CO_2, 3.530 mg H_2O. Found %: C 67.22; 67.20; H 10.87, 10.70. $C_{16}H_{30}O_4$. Calculated %: C 67.10; H 10.56.

The isolated product is the di-α-butoxyethyl ether of butynediol. Yield 64.3% of the theoretical. The residue was brown, viscous liquid.

e) Reaction of butynediol with vinylbutyl ether in the autoclave without catalyst. 60 g (0.7 mole) butynediol and 150 g (1.5 moles) vinylbutyl ether were placed in a 0.5 liter rotating autoclave. The autoclave, while rotating, was heated to 96-110° in the course of 8½ hours. After cooling, the clear liquid product (192 g) was fractionated in vacuum in a stream of dry nitrogen in presence of a crystal of pyrogallol. First fraction, up to 85° at 18 mm, 11 g; second fraction, 85-147° at 18 mm, 6.5 g; third fraction, 147-156° at 18 mm, 28.5 g; fourth fraction, 156-167° at 18 mm, 64.5 g; fifth fraction, 167-170° at 18 mm, 49.0 g; residue 16.2 g. 10 g liquid was condensed in the coil receiver (cooled to −40°).

The first fraction gave a strong reaction for acetaldehyde with fuchsin-sulfurous acid. Butyl alcohol with the following constants was isolated from it by two fractionations: b.p. 117-118°; n_D^{20} 1.3990; d_4^{20} 0.8040.

Dibutylacetal with the following constants was separated from the second fraction: b.p. 185-185.5°; n_D^{20} 1.4095; d_4^{20} 0.8282. These values agree with the literature data [12-14].

The third fraction was butynediol, which crystallized in the receiver and had the following constants after distillation: b.p. 137-137.5° (9 mm); m.p. 57-58°.

On the following day 6 g crystalline butynediol was filtered off from the fourth fraction; two fractionations of the filtrate then gave 5 g of a product with the following constants: b.p. 121-122° (3 mm); n_D^{20} 1.4570; d_4^{20} 0.9745; MR_D 52.05; calculated 51.19.

0.2338 g substance; 18.81 g dioxane: Δt 0.33°. 0.1482 g substance; 18.81 g dioxane: Δt 0.215°. Found: M 188.38, 183.25. $C_{10}H_{18}O_3$. Calculated: M 186.244. 15.26 mg substance: 35.76 mg CO_2; 13.68 mg H_2O. 9.69 mg substance: 22.67 mg CO_2; 8.53 mg H_2O. Found %: C 63.95, 63.76; H 10.03, 9.84. $C_{10}H_{18}O_3$. Calculated %: C 64.49; H 9.74.

The isolated substance is the mono-α-butoxyethyl ether of butynediol.

The residue from the fourth fraction was combined with the fifth fraction and twice distilled in vacuum to give 51.0 g product with the following constants: b.p. 151-152° (2 mm); n_D^{20} 1.4440; d_4^{20} 0.9353; MR_D 81.32; calculated 80.60.

3.73 mg substance: 9.200 mg CO_2; 3.586 mg H_2O. 5.378 mg substance: 13.244 mg CO_2; 5.160 mg H_2O. Found %: C 67.31, 67.21; H 10.85, 10.83. $C_{16}H_{30}O_4$. Calculated %: C 67.10; H 10.56.

The isolated substance is the di-α-butoxyethyl ether of butynediol. Its yield is 60.2% of the theoretical based on the reacted butynediol. The residue is a resinous, transparent, viscous liquid.

f) Preparation of the mono-α-butoxyethyl ether of butynediol. 43 g (0.5 mole) butynediol and 50 g (0.5 mole) vinylbutyl ether were heated in an autoclave in the conditions of the preceding experiment to 96-104° in the course of 1½ hours. 89 g of clear product was discharged and after 3 hours this deposited crystalline butynediol (5 g). The filtrate was fractionated in vacuum: First fraction, 23-120° at 4 mm, 2.9 g; second fraction, 120-127° at 4 mm, 17.1 g; third fraction, 127-134° at 4 mm, 17.8 g; fourth fraction, 134-143° at 6 mm, 6.6 g; residue, 31.1 g (decomposition of the product commenced). Two fractionations of the first fraction yielded dibutylacetal with b.p. 183.5-184.5°; n_D^{20} 1.4085; d_4^{20} 0.8280. The second fraction was butynediol which crystallized in the receiver, m.p. 57-58°. From the third and fourth fractions were isolated 21.8 g mono-α-butoxyethyl ether of butynediol with b.p. 126-127° at 7 mm; n_D^{20} 1.4565; d_4^{20} 0.9750. Yield 38.0% of theory, based on the reacted butynediol.

Ether investigated	Weight of sample (g)	a	b	% acetal
$CH_2O-CH(CH_3)-OC_2H_5$ $C\equiv C$ $CH_2O-CH(CH_3)-OC_2H_5$	0.1540	37.40	10.76	99.60
	0.1564	37.40	10.72	98.22
$CH_2O-CH(CH_3)-OC_2H_5$ $C\equiv C$ CH_2OH	0.2034	37.78	12.34	99.00
	0.1952	37.78	13.49	98.50
$CH_2O-CH(CH_3)-OC_4H_9$ $C\equiv C$ $CH_2O-CH(CH_3)-OC_4H_9$	0.1210	51.75	34.72	100.70
	0.1245	51.75	34.34	100.10
$CH_2O-CH(CH_3)-OC_4H_9$ $C\equiv C$ CH_2OH	0.0904	30.61	9.95	102.40
	1.1200	30.61	17.22	103.80

Hydrolysis of the α-alkoxyethyl ethers of butynediol. Into an Erlenmeyer flask (ground-glass stopper) containing 25 ml 2% sulfuric acid and 25 ml water were introduced a weighed amount (about 0.2 g) of the ether and 25 ml 0.2 N bisulfite solution. The contents of the flask were vigorously shaken for 15 minutes and then allowed to stand for 15 minutes. The excess of bisulfite was then titrated with 0.1 N iodine. The calculation was effected according to the formula:

$$\% \text{ acetal} = \frac{(a-b)\cdot M}{\text{weight of sample}\cdot K},$$

where a is the amount of 0.1 N iodine per ml consumed in titration of 25 ml bisulfite; b is the amount of 0.1 N iodine per ml consumed in titration of the excess of bisulfite in the sample; K = 400 for the diether and 200 for the monoether.

The experimental results are set out in the table.

Hydrogenation of the di-α-butoxyethyl ether of butynediol. 20 g α-butoxyethyl ether of butynediol (b.p. 152-153° at 3 mm) was placed in a "duck" together with 62 g methyl alcohol. The amount of hydrogen taken up after shaking for 2 hours in presence of a catalyst (platinum oxide) was 3.53 l (the theoretical requirement is 3.14 l). After hydrogen had ceased to be taken up (one bubble in 10 minutes), the hydrogenation product was filtered from catalyst, the methyl alcohol was distilled off, and the residue fractionated in vacuum. First fraction 33-37° at 14 mm, 11.8 g; second fraction, 37-120° at 14 mm, 0.2 g; third fraction 120-127° at 14 mm, 3.3 g; residue 0.3 g.

Repeated fractionations of the first fraction yielded butyl alcohol with b.p. 115-116° (756 mm); n_D^{20} 1.3990; d_4^{20} 0.8037.

Three fractionations of the third fraction gave butylene glycol with b.p. 106-107° (3 mm); n_D^{20} 1.4055; d_4^{20} 1.0170; MR_D 23.60; calculated 23.72 [13].

3.325 mg substance: 6.455 mg CO_2; 3.390 mg H_2O. 4.185 mg substance: 8.084 mg CO_2; 4.315 mg H_2O. Found %: C 52.94, 52.71; H 11.41, 11.54. $C_4H_{10}O_2$. Calculated %: C 53.30; H 11.18.

SUMMARY

1. The method of synthesis of butynediol by condensation of acetylene with formaldehyde was improved. The influence of temperature, pressure and catalyst on the course of the reaction was demonstrated and butynediol was obtained in a yield of over 70%.

2. The possibility was established and the conditions found for the synthesis of the mono- and di-α-alkoxyethyl ethers of butynediol.

3. Four α-alkoxyethyl ethers of butynediol, not previously described in the literature, were isolated and characterized: The mono- and di-α-butoxyethyl ethers and the mono- and di-α-ethoxyethyl ethers. Their structure was established by hydrolysis.

4. It was shown that the synthesis of the di-α-alkoxyethyl ethers of butynediol proceeds via the formation of the mono-α-alkoxyethyl ethers whose yield depends on the initial amount of vinyl ether and on the duration of the process.

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REACTIONS OF ALIPHATIC DIAZO COMPOUNDS WITH UNSATURATED COMPOUNDS

XIII. REACTION OF ETHYL DIAZOACETATE WITH ALLYL IODIDE AND WITH NORMAL AND TERTIARY BUTYL BROMIDES IN PRESENCE OF COPPER CATALYSTS

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Following up our investigations in this field [1,2] we have studied the action of ethyl diazoacetate on allyl iodide in presence of copper bronze, using the previously applied procedure. The tendency toward formation of ethyl fumarate during decomposition of ethyl diazoacetate in presence of copper was inhibited by introducing allyl iodide in considerable excess over the quantity required by the equation (1):

$$CH_2{=}CHCH_2I + N_2CHCOOC_2H_5 \xrightarrow{Cu} \underset{(I)}{CH_2{=}CH{-}CH_2CHI{-}COOC_2H_5} + N_2 \qquad (1)$$

It was found that equation (1) represents the main direction of the reaction.

The crude ester (I) was isolated in a yield of 70% of theory and the analytically pure substance in 47% yield. Serious losses arose in purifying the crude preparation, due to the low thermal stability of ester (I) and to contamination with traces of ethyl iodoacetate $ICH_2COOC_2H_5$ (II). The latter could not be isolated but its presence was manifested by the strong lachrymatory effect. Further evidence of its presence was obtained by the results of dehalogenation of the lower boiling fraction of the crude iodine-containing preparation (dehalogenation yielded a mixture of acetic and allylacetic acids, corresponding in composition to the initial mixture of ethyl bromoacetate and ethyl bromoallylacetate).

Ester (I) differed from the esters of α-bromo- [1] and α-chloroallylacetic acids [2] previously prepared by us, also in its behavior toward aqueous alkali solutions. Whereas the chloro- and bromo-esters, as previously shown [1,2] yield predominantly α-hydroxyallylacetic acid when heated with 10% potassium carbonate and only an insignificant amount of vinylacrylic acid, ethyliodoacetate (I) in the same conditions gives mainly vinylacrylic acid (III) or its polymer (equation 2).

Allylhydroxyacetic acid (IV), obtained in negligible yield, was characterized in the form of its anilide:

$$(I) \xrightarrow[K_2CO_3]{60\%} \underset{(III)}{(CH_2{=}CH{-}CH{=}CH{-}COOH)} \longrightarrow \underset{\text{polymer}}{(C_5H_6O_2)_x}$$
$$(I) \xrightarrow[H_2SO_4]{\text{traces}} \underset{(IV)}{CH_2{=}CH{-}CH_2{-}CHOH{-}COOH} \xrightarrow{C_6H_5NH_2} \underset{\text{anilide}}{C_{10}H_{11}NO_2} \qquad (2)$$

Reduction with hydrogen of ester (I) in an acetic acid medium gave the ester of allylacetic acid (V) which has been described in the literature [7] and which we obtained by the analogous reduction of the ester of α-bromoallylacetic acid [1]. The structure of ester (V) was confirmed by permanganate oxidation which yielded succinic and acetic acids:

$$(I) \xrightarrow[(65\%)]{H_2} \underset{(V)}{CH_2{=}CHCH_2CH_2COOC_2H_5} \xrightarrow[46\%]{KMnO_4} HOOCCH_2CH_2COOH + CH_3COOH + CO_2 \qquad (3)$$

The transformations of ester (I) represented by equations (2) and (3) not only characterize its properties but also confirm its structure.

Normal and tertiary butyl bromides do not react with ethyl diazoacetate in presence of copper catalysts with formation of the esters of the corresponding α-bromo acids, as would have been expected by analogy with

the cases previously investigated by us. With n-butyl bromide the sole reaction product was ethyl fumarate; in the case of tert. butyl bromide, ethyl bromoacetate (VIII) was obtained in addition to ethyl fumarate.

We explain the formation of this substance by cleavage of hydrogen halide from the ester of α-bromo-isovaleric acid (VI) formed in the first place and which at once rearranges into the ester of trimethylacrylic acid (VII):

$$(CH_3)_3CBr \xrightarrow[(CuSO_4)]{N_2CHCO_2C_2H_5} \underset{(VI)}{[(CH_3)_2CCHBrCOOC_2H_5]} + N_2; \qquad (4)$$

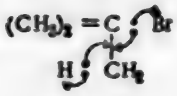
$$\xrightarrow{N_2CHCO_2C_2H_5} \underset{(VII)}{\left[(CH_3)_2C{=}\underset{\displaystyle CH_3}{\underset{|}{C}}COOC_2H_5\right]} + \underset{(VIII)}{CH_2BrCOOC_2H_5} + N_2. \qquad (5)$$

Only ethyl bromoacetate (b.p. 159°) was isolated from the reaction products; it was freed from the conjectured trimethylacrylic acid (b.p. 155°) by treatment with cold potassium permanganate solution. After this treatment the bromine content was still lower than the calculated value; conclusive evidence of the structure was obtained by conversion of a portion of the material into acetic acid by reductive dehalogenation in an alkaline medium.

Taking into account the previous [1,3] ideas about the radical mechanism of heterogeneous catalytic reactions of ethyl diazoacetate, we may suggest that the rupture of the C–Hal bond in allyl halides during attack on the alkylene radical $\rangle CH{-}COOC_2H_5$ will promote the effect of the homolytic conjugation of the σ–π-bonds [4] (A).

(A)

The magnitude of this effect must be inversely proportional to the electronegativity of the halogen atom in the allyl halide, i.e., I > Br > Cl. The experimental data are in satisfactory agreement with this order, judging by the yields of the corresponding α-haloallylacetic esters in the investigated reaction: I- and Br-esters about 70%; the Cl-ester 10.9% of the theoretical yield.*



(B)

In tert.-butyl bromide the homolytic effect of conjugation is also apparently sufficient for development of a similar reaction but on a very much smaller scale than with allyl halides (B).

In n-butyl bromide this effect is not manifested during attack of the alkylene radical.

The mechanism of formation of haloacetic esters demands another explanation. As we know, ethyl diazoacetate (in noncatalyzed reactions) may detach the elements of hydrogen halides from some esters of halo-substituted liquid acids with formation of the corresponding haloacetic esters [5]. We suggest that in the present case also the haloacetic esters are formed by reaction of ethyl diazoacetate, which has failed to come into contact with the copper, with the α-haloallylacetic esters formed according to the proposed catalytic scheme. Since ethyl diazoacetate in itself is not a reagent of the radical type but rather of the nucleophilic type (binding, for example, a proton to the unstable diazonium cation $N_2CH_2COOC_2H_5^+$ [6]), then the formation of haloacetic esters must apparently proceed through heterolytic rupture of the C–Hal and C–H bonds in the molecule of the original haloallylacetic ester.

In the case of allyl bromide and iodide the yields of haloacetic esters are very low (about 1% of theory), which may be explicable on the basis of more successful competition in these cases of the homolytic reaction with participation of the free alkylene radical $\rangle CHCOOC_2H_5$. In the case of allyl chloride and tert.butyl bromide the main (radical) reaction proceeds less energetically, and consequently higher yields of haloacetic esters are obtained: $ClCH_2COOC_2H_5$ – 9.8% and $BrCH_2COOC_2H_5$ – 9.1% of the theoretical yield.

* Calculated on the crude preparation.

EXPERIMENTAL

1. Condensation of ethyl diazoacetate with allyl iodide. 560 g dry, freshly distilled allyl iodide and 0.8 g copper bronze ("Natur Cupfer C") are introduced into a three-necked round-bottomed flask fitted with mechanical stirrer, dropping funnel and reflux condenser. The allyl iodide is heated to the boil, the stirrer is started up, and a solution of 175 g ethyl diazoacetate in 175 g allyl iodide is run in from the dropping funnel. The nitrogen evolved during the reaction is collected in a gasholder after passing in succession through a reflux condenser and a trap immersed in freezing mixture. At the end of the reaction 29.5 l nitrogen (18°, 767 mm) had been evolved, which was equivalent to 79.3% of the theoretical amount. The reaction product, after cooling, is filtered from catalyst, and the excess allyl iodide is distilled off at 100 mm. The residue in the distillation flask (a dark-colored liquid) is distilled in a 4 mm vacuum. Partial decomposition of the material occurred during the distillation with cleavage of molecular iodine which imparted a reddish color to the distillate. The yield of crude ethyliodoallyl acetate (I) with b.p. 65-82° at 4 mm was 274.3 g (70% of the theoretical).

Vacuum fractionation of crude ester (I)

No. of fraction	Boiling range	n_D^{20}	Weight (g)
1	77-90° at 12 mm	1.4945	6.3
2	49-66° at 1 "	1.4950	10.4
3	56-65° at 1 "	1.5005	9.5
4	65-66° at 1 "	1.5062	183.7

The undistillable residue weighed 60 g (resinified products). The crude reaction product was repeatedly fractionated in vacuum for isolation of the pure ester (I). The molecular iodine released during the distillations was removed from the distillate by shaking with mercury.

Fraction 4 is the analytically pure preparation of ester (I) (yield 47% of theory). Fractions 1-3 were assumed to be a mixture of the esters of iodoacetic and iodoallylacetic acids. The first of these was subjected to reductive dehalogenation for the purpose of obtaining acetic acid and so demonstrating the presence of iodoacetic acid in this fraction.

5.7 g of the material of Fraction 1, 10 ml water and 45 g 30% sodium amalgam were shaken for 3 hours under external cooling. After the mercury had been separated, the solution was boiled for 4 hours with 200 ml 5% potassium hydroxide solution. The cooled alkaline solution was acidified with tartaric acid (30 g) and the volatile acids distilled off with steam.

Fractional precipitation with $AgNO_3$ solution of the neutralized alkaline distillate gave three fractions of silver salts which were analyzed for their silver content.

Found %: Ag I 54.82, 55.13; II 58.12, 58.42; III 60.29. $C_3H_5O_2Ag$. Calculated %: Ag 52.13. $C_2H_3O_2Ag$. Calculated %: Ag 64.66.

II. Ethyl α-iodoallylacetate. A colorless oil with a pleasant ethereal odor; b.p. 62-66° at 1 mm.

d_4^{20} 1.558; n_D^{20} 1.5062; MR_D 48.45; calculated 48.51. 0.2248 g, 0.3641 g substance: 0.2088 g, 0.3385 g AgI. 0.3799 g, 0.1618 g substance; 21.21, 20.58 g C_6H_6; Δt 0.39°, 0.16°. Found %: I 50.23, 50.25; M 235.6, 251.7. $C_7H_{11}O_2I$. Calculated %: I 49.97; M 254.0.

Dehalogenation. To a mixture of 60 g ester (I), 60 ml alcohol and 90 g 65% acetic acid, heated on a water bath to 65°, was added 20 g zinc dust in small portions. The mixture was then refluxed for one hour, the unreacted zinc dust was filtered off after cooling, the solution neutralized with soda, and the ester was extracted with ether.

The ethereal solution was dried with sodium sulfate; the ether driven off and the residual ethyl allylacetate distilled in vacuum. The yield of ester with b.p. 43-44° at 12 mm [7] was 19.7 g (65.2% of the theoretical yield).

d_4^{19} 0.9016; n_D^{20} 1.416; MR_D 35.67; calculated 35.71.

0.2180 g substance: 0.5225 g CO_2; 0.1859 g H_2O. Found %: C 65.36; H 9.53. $C_7H_{12}O_2$. Calculated %: C 65.58; H 9.43.

Oxidation of the ester with potassium permanganate. 10 g of the ester was treated in the cold with 3% $KMnO_4$ solution. 20.9 g of permanganate was consumed. After the usual treatment the nonvolatile and the steam-volatile acids were separated by the usual method. The steam-volatile acids were examined in the form of their silver salts.

0.0934 g substance: 0.0605 g Ag. Found %: Ag 64.79. $C_2H_3O_2Ag$. Calculated %: Ag 64.66.

Succinic acid was found in the solution of the acids non-volatile in steam. Yield 46% of the theoretical. M.p. 182°. It did not depress the melting point of an authentic sample of succinic acid.

0.1665 g substance: 27.93 ml 0.1 N NaOH. Found: equiv. 59.61. $C_4H_6O_4$. Calculated: equiv. 59.0.

Hydrolysis of ester (I). 50 g of ester (I) was hydrolyzed by heating with 10% potassium carbonate solution under good stirring. The resultant solution was concentrated to a volume of 150 ml, acidified with sulfuric acid until acid to Congo, and extracted with ether in a Soxhlet. The ethereal extract yielded 16.5 g viscous, yellow oil which partially crystallized when cooled with a freezing mixture. On attempted filtration the crystals deliquesced on the filter. It was only possible to isolate an insignificant amount of colorless, prismatic crystals which after standing for 12 hours in a vacuum desiccator were converted into a resinous mass of polymer. We assumed that the latter was a polymer of vinylacrylic acid and that the crystals were the monomer. The polymer dissolved when heated in alkalies and again came down when acidified*

0.1850 g substance: 36.4 ml 0.1 N NaOH. Consumed 18.7 ml 0.1 N HCl. Found: equiv. 104.6 $(C_6H_8COOH)_x$. Calculated: equiv. 98.1.

The residual oil polymerized almost completely after standing for five days, giving 10 g polymer. The unpolymerizable portion of the oily acid was extracted with ether. The very small quantity of liquid acid obtained after evaporation of the ether was characterized by conversion into the anilide by the method developed for the preparation of anilides of monocarboxylic acids and their sodium salts [9]. The unrecrystallized anilide melted at 74-75°. Its mixture with the anilide of authentic α-hydroxyallylacetic acid (m.p. 77-78° [2]) melted at 75-76°. The investigated acid was therefore assumed to be hydroxyallylacetic acid.

III. Action of ethyl diazoacetate on tert. butyl bromide in presence of copper sulfate. Using the procedure and apparatus described in part I above, 360 g freshly distilled tert. butyl bromide, 0.5 g anhydrous copper sulfate and 135.7 g ethyl diazoacetate were brought into reaction.

After distilling off the excess butyl bromide, the reaction product was distilled in a 5 mm vacuum. A considerable amount of resinous material remained in the distilling flask and two liquid fractions were obtained: I with b.p. 35-65° at 5 mm (20.9 g) and II with b.p 55-80° at 5 mm (38.7 g).

Examination of fraction I. It was intensely lachrymatory and contained halogen. Fractionation in a column at normal pressure yielded 15.1 g substance with b. p. 156-160°.

n_D^{18} 1.4455; d_4^{20} 1.414.

0.1467 g substance, 0.1241 g AgBr. Found %: Br 35.99. $C_4H_7O_2Br$. Calculated %: Br 47.84.

The constants of ethyl bromoacetate reported in the literature [10] are: b. p. 159°; d_4^{13} 1.51414; n_D^{13} 1.45420.

Unsaturated impurities in the investigated fraction were removed by shaking in the cold with 3% permanganate solution (the permanganate consumption was 1 g for 14.5 g substance). After vacuum distillation the substance had b p. 156-160°; n_D^{15} 1.4485.

0.3030 g, 0.2985 g substance: 0.0989 g, 0.0985 g AgBr. 0.1666 g, 0.3376 g substance; 15.05, 15.05 g C_6H_6: Δt 0.37°, 0.74°. Found %: Br 41.93, 42.38; M 153.5, 155.5. $C_4H_7O_2Br$. Calculated %: Br 47.84, M 167.0.

The material of fraction I was dehalogenated in the above manner. Only acetic acid was detected in the dehalogenation product after hydrolysis. It was identified through the silver salt:

0.1102, 0.1371 g salt: 0.0713, 0.0879 g Ag. Found %: Ag 64.71, 64.12. $C_2H_3O_2Ag$. Calculated %: Ag 64.66.

Examination of fraction II. Fractionation gave 20.2 g liquid with the characteristic odor of ethyl fumarate and boiling at 65° at 1.5 mm; d_4^{20} 1.0593; n_D^{20} 1.4410. The literature [11] gives b. p. 96° at 10 mm; n_D^{20} 1.4410; d_{20}^{20} 1.0535. The identity was confirmed by saponification with potassium hydroxide in methyl alcohol to form a precipitate of potassium fumarate; from the latter, diphenacyl fumarate was prepared with m. p. 197° (the literature [12] reports 197°). It did not depress the melting point of a sample of authentic diphenacyl ester.

IV. Action of ethyl diazoacetate on n-butyl bromide in presence of copper bronze. Condensation of 68

* According to the literature [8] the monomer of vinylacrylic acid forms colorless, very hygroscopic prisms with m.p. 80°. Readily soluble in alcohol and water. On standing it polymerizes to a solid polymer.

ml n-butyl bromide with 11.4 g ethyl diazoacetate was performed by the usual procedure (see section I above) in presence of 0.5 g copper bronze. The catalyst was then filtered off and the unreacted butyl bromide (63 ml) was distilled off at 142 mm. The weight of the residue in the distilling flask was 10.2 g. Fractionation of this residue at 9 mm gave 3.2 g liquid with the odor of ethyl fumarate and b. p. 91-92°; n_d^{20} 1.437 (yield 37.2%). The weight of unreacted residue was 6.9 g.

Literature constants for ethyl fumarate [11]: b. p. (10 mm) 96°; n_d^{20} 1.437625.

SUMMARY

1. It is shown that reaction of ethyl diazoacetate with allyl iodide in presence of copper powder gives about a 70% yield of α-iodoallylacetic ester together with an insignificant amount of ethyl iodoacetate.

2. Some reactions of ethyl α-iodoallyl acetate were studied and the results were compared with those of similar experiments with chloro- and bromoallyl acetic esters.

3. Condensation of ethyl diazoacetate with tert.- and n-butyl bromides led to isolation in the first case of the esters of fumaric and bromoacetic acids and in the second case of only the ester of fumaric acid. It is suggested that the ester of α-bromoisovaleric acid is formed as an intermediate product in the reaction with tert.-butyl bromide.

4. A reaction mechanism is proposed for the formation of haloallylacetic and haloacetic esters in the reaction of ethyl diazoacetate with alkyl halides in presence of copper catalysts.

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THE STRUCTURE OF OLEIC ACID

A. K. Plisov and E. G. Maleeva

The structure of the geometrically isomeric monobasic acids has not yet been definitely established, and even such familiar acids as oleic and elaidic are sometimes regarded as cis-isomers and sometimes as trans-isomers [1].

The problem of the determination of the cis- and trans-isomers of aliphatic and cyclic compounds is an extremely difficult one. When the molecule of the substance contains two radicals capable of acting on each other, the formation of an intramolecular derivative (anhydride, lactam, etc.) is characteristic of cis-isomerism. Apart from such clearly definable cases, up to recent times no other criteria were available except the definition of a trans-isomer as a substance which is more stable, has a higher melting point and is chemically less active. These criteria spring from analogy with certain cases which are known to be unrelated to the present cases. Nevertheless it is already clear than even these methods are not universally applicable. Thus, some trans-forms are known whose melting points are lower than those of the isomeric cis-forms. We could cite a long list of fundamental attempts to find a valid method for determining the actual structure of cis- and trans-isomeric compounds. This clearly demonstrates how difficult is the problem and how few solutions have been obtained.

One of the present authors once suggested that on the basis of the theory of steric hindrance we should expect different reactivities on the part of geometrical isomers and their derivatives. In that event a chemical solution should be possible of the problem of the true configuration of unsaturated compounds with cis-trans isomerism (a hitherto unsolved problem) if we consider those derivatives of acid which do not contain groups readily capable of reacting intramolecularly with one another.

Considering the case of oleic acid and its derivatives such as esters, we may assume on the basis of the theory of steric hindrance that all reactions associated with the double bond of the cis-form, such as addition of hydrogen, halogens, hydrogen halides and oxygen must proceed more readily than in the case of the trans-form, in which the action on the double bond of molecules of reactants will be hindered by the $CH_3(CH_2)_7$ and $(CH_2)_7COOH$ radicals which block the space near the double bond from two sides. This crowding does not occur to the same extent in the cis-form where both radicals are attached at one side of the double bond. Concerning reactions involving the carboxyl group of oleic acid or its esters, the reaction of a molecule of an alcohol with the carboxyl group or that of alkali with the ester group will proceed more readily in the trans-form and will be hindered in the cis-form, because the space in the vicinity of the carboxyl or ester group in the cis-form is occupied by the radical $CH_3(CH_2)_7$, and molecules of alcohol or alkali must first overcome the hindrance created by the hydrocarbon radical. This difficulty will not arise with the trans-form. Consequently the esterification of oleic acid and the saponification of its esters should proceed with greater difficulty in the case of the cis-form than in the case of the trans-form. Esterification or saponification of the esters may possibly proceed in the cis-form the more slowly the more branched is the alcohol radical. We must assume that the entry of a radical into the molecule introduces something more than just congestion of the space: it introduces what we may call the chemical effect of the radical. The chemical effect can vary substantially with the reactions, some of which are hindered while others are facilitated. Concerning the steric effect, it comes into play – if not always with equal intensity then at any rate in some degree – for all reactions which take place directly at the group in question. The resultant of both effects is the same and is accessible to experiment. In some cases this resultant may have a reverse effect in relation to the steric effect. When a compound contains radicals with a weakly manifested chemical individuality, e.g., alkyls, the chemical effect will be weak and hardly capable of opposing steric hindrance. Applying the theory of steric hindrance to cis- and trans-forms, in the case under consideration we can expect definite assistance from it: the chemical effect of the radical will be sufficiently similar in both isomers, but the steric effect will be considerably different.

We have studied the reactions of oxidation and hydrogenation [2] of oleic and elaidic acids and the saponification, hydrogenation and oxidation of methyl oleate and methyl elaidate. The velocities of these reactions were found to differ in methyl oleate and methyl elaidate. Methyl oleate is saponified more slowly than elaidate but is oxidized and hydrogenated more rapidly than elaidate.

The results make it appear that a cis- and trans-structure must be, respectively, ascribed to oleic acid (and methyl oleate) and elaidic acid (and methyl elaidate).

EXPERIMENTAL

The methyl esters of oleic and elaidic acids were prepared from the pure silver salts of the acids and methyl iodide and had the following constants:

Methyl oleate. b. p. 213–213.5° at 15mm; d_4^{16} 0.8780;

K_0 189 (calculated K_0 189.1) $K_p 0$.

Methyl elaidate: b. p. 214° 15 mm; d_4^{16} 0.8790; K_0 189; $K_p 0$.

1. Determination of relative velocities of saponification of methyl oleate and methyl elaidate. Each ester was weighed out in quantity of 0.1480 g (1/2000M) into a small glass cylinder with a ground-glass stopper into which were sealed two platinum electrodes. Addition was made of 5 ml 96% alcohol and 5 ml 0.1 N alcoholic KOH and a first determination of electric conductivity was made with the help of a resistance bridge and a lamp-type optical indicator. Each experiment was assumed to start from the instant of addition of the alcoholic potash to the ester; then at definite intervals of time the electric conductivity of the alcohol solution was measured at a temperature of 25°, the conductivity being a direct measure of the hydroxyl ion concentration. The significant feature in this connection is the fall in conductivity, i.e., the fall in conductivity during a specified interval of time. In the present case the fall of electric conductivity depends on the reaction between alkali and ester (during which the hydroxyl ions which are responsible for the good conductivity of the solution gradually disappear and are replaced by the salts of oleic or elaidic acid which are characterized by poor conductivity). The ester and glycerol do not exert an important influence on the electric conductivity so that the fall in electric conductivity is a measure of the progress of the saponification reaction.

In Table 1 are set out the results of measurement of the electric conductivity of the reaction medium during saponification of the methyl esters of oleic and elaidic acids.

TABLE 1

No.	Duration of experiment (minutes)	Electric conductivity $\cdot 10^4$	Fall of electric conductivity	Maximum change in electric conductivity as % of the initial conductivity
	Saponification of methyl oleate			
1	0	555	–	12
	30	512	43	
	90	488	67	
	150	486	69	
2	0	500	–	12
	30	454	46	
	90	434	66	
	150	430	70	
	Saponification of methyl elaidate			
3	0	500	–	17
	30	454	46	
	90	434	66	
	150	412	88	
4	0	555	–	16
	30	500	55	
	90	474	81	
	150	465	90	

Similar results were obtained in saponification experiments carried out at a temperature of 28°.

2. Hydrogenation of methyl esters of oleic and elaidic acids. Hydrogenation was effected in presence of platinum deposited on $BaSO_4$; materials used in each experiment were 0.25 g $BaSO_4$ and 0.008 g metallic platinum, 15 methyl alcohol and 0.8 g methyl oleate or elaidate. Experiments were run simultaneously with the two esters at 25° in a hydrogenation "goose." Blank experiments with pure oleic and elaidic acids were run in order to establish the degree of activity of the catalyst and for the purpose of comparison. Hydrogenation results are in Table 2.

Oxidation of oleic and elaidic acids and of their methyl esters. Oxidation was studied by the reaction with potassium permanganate when, as we know, both acids react to form the dihydroxystearic acids. We found that oleic and elaidic acids react with potassium permanganate at different speeds. The course of the

oxidation could be followed by the change in electric conductivity of the $KMnO_4$ solution, the conductivity rising appreciably with progressive consumption of the oxidizing agent, since the place of the decomposed $KMnO_4$ was taken by molecules of KOH which are known to possess a higher conductivity.

TABLE 2

Duration of hydrogenation in minutes from start of expt.	ml H_2 absorbed (a)			
	oleic acid	elaidic acid	methyl oleate	methyl elaidate
20	48	37	46	35
40	81	72	80	70
60	104	90	103	90

$$\frac{a_{oleate}}{a_{elaidate}} = \frac{103}{90} = 1.14:1;$$

$$\frac{a_{oleic\ acid}}{a_{elaidic\ acid}} = \frac{104}{90} = 1.15:1.$$

In the present case, therefore, the rising electric conductivity of the $KMnO_4$ solution in contact with the oleic or elaidic acid or their esters served as a criterion of the decomposition velocity of $KMnO_4$ and in turn of the velocity of the oxidation reaction. Concerning the formation during this reaction of the salt of the organic acid at the expense of the alkali formed during deoxidation of the $KMnO_4$, this process here proceeds so slowly that it has no substantial effect on the measurement of the electric conductivity of the solution.

The oxidation experiments were performed simultaneously with identical weights of the acids and esters (1/5000 mole) introduced as in the saponification experiments in identical vessels fitted with platinum electrodes. To each of the samples was added 5 ml 1.5% aqueous $KMnO_4$ solution and the first determination of electric conductivity was quickly made. Before the mixing, each reagent had been kept in a thermostat for 15 minutes. Oxidations of the acids were performed at 48° and those of the esters at 25°. Table 3.

TABLE 3

Number of experiment	Duration (minutes)	Electric conductivity $\cdot 10^4$	Increase in electric conductivity	Maximum change in electric conductivity in % of initial conductivity
		Oxidation of oleic acid		
1	0	514	–	38.9
	15	666	152	
	30	714	200	
	45	714	200	
		Oxidation of elaidic acid		
2	0	514	–	26.2
	15	598	84	
	30	647	133	
	45	649	135	
		Oxidation of methyl oleate		
3	0	430	–	19
	30	446	16	
	60	472	42	
	120	488	50	
	180	511	81	
		Oxidation of methyl elaidate		
4	0	434	–	12.4
	30	444	10	
	60	454	20	
	120	476	42	
	180	488	54	

SUMMARY

1. It is establish that oleic and elaidic acids and their methyl esters exhibit different reactivities.

2. Methyl elaidate is saponified more rapidly than methyl oleate.

3. Elaidic acid and its methyl ester are hydrogenated and oxidized with greater difficulty than oleic acid and its methyl ester.

4. The reactivity of oleic and elaidic acids and their methyl esters is consistent with the theory of steric hindrance and confirms their structure as, respectively, cis- and trans-isomers.

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DIRECT SYNTHESIS OF ALKYL- AND ARYLHALOSILANES

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The preparation of alkyl- and arylhalosilanes by the action of haloalkyl(aryl) derivatives on silicon in presence of a catalyst was first described in 1945 [1]. This reaction gives a mixture of halogen-containing organosilicon compounds with various ratios of halogen to organic radical, namely, $RSiX_3$; R_2SiX_2; R_3SiX; SiX_4; SiR_4, etc. R is an organic radical and X is halogen.

These compounds are formed according to the following schemes:

1. $2RX + Si \rightarrow R_2SiX_2$;
2. $3RX + Si \rightarrow R_3SiX + X_2$;
3. $3RX + Si \rightarrow RSiX_3 + 2R$;
4. $2X_2 + Si \rightarrow SiX_4$;
5. $4RX + 2\,Si \rightarrow SiR_4 + SiX_4$.

Depending on the conditions the main product will be various halo-substituted alkyl- and arylsilanes, especially R_2SiX_2.

The lowest temperature at which this reaction commences is the optimum for the addition of an organic radical to silicon; with rising temperature the reaction velocity increases but at the same time the final mixture of products becomes richer in halogen, until $SiCl_4$ is reached, and correspondingly poorer in carbon and hydrogen. The reaction velocity also depends on the nature of the organic radical, of the halogen and of the catalyst.

Of great importance for obtaining good yields of alkyl- and arylhalosilanes is the quality of the catalyst. Copper is an active catalyst in the reaction of silicon with alkyl and aryl halides. It accelerates the reaction and permits operation at a lower temperature, although the role of copper in the mechanism of this reaction is still not altogether clear.

A direct synthesis has been utilized industrially for the production of methylchlorosilanes and phenylchlorosilanes [2]. In our research we set ourselves the task of studying the direct synthesis of methylbromosilanes and phenylbromosilanes [3,4].

The work was carried out in the department of organic and petroleum chemistry of the Acad. I. M. Gubkin M N.I.* in 1946-1947 (synthesis of methylbromosilanes) and in 1949 (synthesis of phenylbromosilanes). During the completion of this research a short publication appeared [5] which gave a brief description of the preparation of methylbromosilanes and of their analysis.

EXPERIMENTAL

Methyl bromide was reacted with silicon also bromobenzene with silicon in an apparatus consisting of a tube furnace (electrically heated) 0.8 meter long and 40 mm in internal diameter. Two molybdenum glass tubes 1.2 meters long and 15 mm in diameter were inserted in this furnace. Each tube was charged with an intimate mixture of 60 g (80%) silicon and 15 g (20%) reduced copper. The silicon was previously ground to a fine powder in a porcelain mortar. The copper was reduced from copper oxide powder at 300°. The air was displaced from the system with carbon dioxide prior to starting the passage of methyl bromide (for preparation of methylbromosilanes) and of bromobenzene (for preparation of phenylbromosilanes).

Preparation of methylbromosilanes. Preliminary experiments showed that at 250-300° the reaction of methyl bromide with silicon in presence of copper was not sufficiently energetic; systematic experiments were therefore run at temperatures of 320-360°. Table 1 gives the yields of methylbromosilanes at various temperatures.

We see from the table that the best yields are obtained at 330-340°, although deviations of 10° to either side of this range did not cause large changes in yields.

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The rate of passage of methyl bromide is an important factor; if it is too high a large proportion of the methyl bromide fails to react in the tubes and is absorbed in the receivers, which reduces sharply the yields of crude reaction product and leads to heavy losses during fractionation, mainly due to the volatility of the methyl bromide (see experiments 2 and 3, Table 1).

TABLE 1

Formation of Methylbromosilanes at Various Temperatures

No.	Methyl bromide consumed (g)	Temperature of experimental series (°C)	Duration of experiment (hours)	Weight of reaction product		Losses (%)
				before fractionation (in g)	after fractionation of the organosilicon compounds (in g)	
1	1250	320-330	48	648.6	507.3	21.9
2	1250	330-340	57	654	569	11.5
3	1250	330-340	42	823.6	618	25.4
4	1120	350-360	48	620	486	21.5

In otherwise equal conditions the velocity of the reaction appreciably increases on the second day of an experiment, i.e., about 10-12 hours after the start of the series of experiments, this is probably associated with the fact that the reaction mass (silicon + copper) has by that time become more porous, in consequence of which the surface of the reaction zone is increased. On the third day, however, the total yield of reaction product falls appreciably and continues to fall up to the end of the given series of experiments due to gradual consumption of the silicon.

The data of Table 2 illustrate the progress of the reaction in four series of experiments at temperatures of 310-320°, 320-330°, 330-340° and 350-360°.

TABLE 2

Course of Formation of Methylbromosilanes at Various Temperatures

No.	310-320°			320-330°			330-340°			350-360°		
	Duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)	duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)	duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)	duration of experiments (hours)	consumption of methyl bromide (g)	wt. of product (g)
1	12	280	152.4	12	280	119.5	11	250	190	12	280	149
2	12	280	166.5	12	280	182.6	9	250	247.3	12.5	280	246
3	12	280	90	12	280	105.3	7	250	168.7	12	280	137
4	12	280	71.7	12	280	114.4	7.5	250	140.6	12	280	86
5	12	280	63	12	280	74.3	7.5	250	77	—	—	—
Total	60	1400	543.6	60	1400	599.1	42	1250	823.6	48.5	1120	620

Composition of the products of reaction of methyl bromide with silicon. In order to establish the composition of the gaseous products which volatilized during fractionation, we distilled the mixture of methylbromosilanes without changing the receivers, to 140°, i.e., to the temperature usually reached in our fractional distillations. The receiver was a Wurtz flask whose exit tube was connected to traps which collected the gaseous products. A water, scrubber was the first trap and was separated from the receiver by a calcium chloride tube; the connecting tube of this scrubber was above the surface of the water in order to avoid sucking back. This scrubber was intended for absorption of the hydrogen bromide which our observations showed to be evolved during fractionation. The scrubber was followed by two absorbers which were cooled to −20° with ice-salt mixture. These were intended for condensation of any methyl bromide (b. p. +4°) which did not enter into reaction and which dissolved in large quantity in the mixture of methylbromosilanes.

After several such fractionations of the reaction product we were satisfied that the main portion of the volatile products consisted of methyl bromide. Its quantity was found to depend on the reaction temperature and the rate of flow of the methyl bromide through the reaction zone: the lower the reaction temperature (for a given rate of flow) the greater the amount of methyl bromide in the reaction product. For example, in one experiment

performed at 300-310°, after fractionation there was obtained methyl bromide in amounts equivalent to 17% of the product taken for fractionation. In another experiment at 350-360° and the same flow velocity the amount of methyl bromide recovered unchanged was only about 7% of the weight of reaction product fractionated.

It was also established that hydrogen bromide came over and was collected in the water scrubber. After fractionation this scrubber increased considerably in weight. Titration showed that the mean amount of hydrogen bromide was about one percent of the product which was fractionated. About 3% of the volatiles (calculated on the weight of fractioned product) was lost. These may have been the simplest, very volatile substituted silanes formed as by-products of the reaction.

With the aim of isolating the individual methylbromosilanes in the purest possible form we subjected the mixture of crude products to repeated fractionation. All attention was concentrated on the isolation of fractions corresponding to trimethylbromosilane, dimethylbromosilane and methyltribromosilane.

Trimethylbromosilane $(CH_3)_3SiBr$ (b. p. 80°, bromine content 52.21%). Our attempts to obtain this most volatile methylbromosilane have so far given negative results. The fraction with a five-degree boiling range (77-82°) in which we expected to find trimethylbromosilane was analyzed for bromine (Volhard method) and found to contain a higher proportion of bromine (56% or more), apparently due to impurities with a higher bromine content, such as dimethyldibromosilane, etc. In view of the fact that this fraction was extremely small it was impossible to examine it more closely.

We determined the bromine content of the methylbromosilanes by Volhard's method, modified to suit the special case, i.e., after hydrolysis of the bromo compound.

Dimethyldibromosilane $(CH_3)_2SiBr_2$ is the main product of reaction of methyl bromide with silicon. We isolated it in the pure state.

B. p. 112-112.5° (760 mm.) Literature data: b. p. 112.3°. 0.6338 g substance: 4.65 ml 0.1 N $AgNO_3$. 0.7282 g substance: 5.35 ml 0.1N $AgNO_3$. 0.7430 g substance: 5.45 ml 0.1N $AgNO_3$. Found %: Br 73.29, 73.29, 73.28. $C_2H_6SiBr_2$. Calculated %: Br 73.33

Methyltribromosilane CH_3SiBr_3 was isolated in the pure state.

B. p. 133-133.5° at 755 mm; literature data: b. p. 133.5° at 764 mm. 0.9322 g substance: 7.9 ml 0.1N $AgNO_3$. 0.5440 g substance: 4.6 ml 0.2N $AgNO_3$. Found %: Br 84.66, 84.48. CH_3SiBr_3. Calculated %: Br 73.33.

Higher fractions (boiling above 140°). Whereas all the above-described methylbromosilanes were colorless after distillation, the residue following their separation had a dark color (ranging from dark-brown to nearly black). The Volhard determination of bromine (mean of several analyses) in the residue gave a value of 63.5%. On attempting to fractionate this residue we succeeded in isolating a small number of fractions with the boiling point of silicon tetrabromide (151°), after which the temperature rapidly rose to above 200° due to the presence of some more complex products of condensation or polymerization.

General properties of the methylbromosilanes. All the methylbromosilanes are heavy liquids. They fume in the air and are hygroscopic. They etch glass and carbonize cork. A conspicuous feature is the regular change in boiling point with increasing bromine content (Table 3).

TABLE 3

Boiling Points of Methylbromosilanes

	$(CH_3)_3SiBr$	$(CH_3)_2SiBr_2$	CH_3SiBr_3	$SiBr_4$
Boiling point	79.9°	112.3°	133.5°	151°

TABLE 4

Boiling points of Methylchlorosilanes

	$(CH_3)_3SiCl$	$(CH_3)_2SiCl_2$	CH_3SiCl_3	$SiCl_4$
Boiling point	57.6°	70°	66°	59°

This regularity contrasts with the variation of boiling points of the methylchlorosilanes shown in Table 4: with increasing chlorine content the boiling point at first rises and then (starting from methyltrichlorosilane) begins to fall, so that the boiling point of tetrachlorosilane is only 1.4° higher than that of trimethylchlorosilane.

Preparation of the phenylbromosilanes*. Preliminary experiments on

* N.M. Zhmykhova participated in the synthesis of the phenylbromosilanes.

the preparation of the phenylbromosilanes showed that the reaction of bromobenzene with silicon was not sufficiently energetic at temperatures below 400°. The yield of organosilicon compounds was about 20%. Systematic experiments with the aim of establishing the optimum reaction temperature were therefore carried out at temperatures of 400-500° (Table 5).

TABLE 5

Preparation of Phenylbromosilanes at Various Temperatures

No. of preparation	C_6H_5Br passed through (in g)	Temp.	Duration of expt. (hours)	Wt. of reaction products (g)	Amount of organosilicon compounds	
					(in g)	(in %)
1	700	400-410°	70	686	324.8	47.4
2	700	410-420	56	662.1	374.6	56.5
3	700	420-430	51	659.4	336.9	51
4	700	440-460	56	684.5	348.1	50.8
5	700	480-500	91	532.6	258	48.4

The table shows that the best yields of phenylbromosilanes are obtained at temperatures of 410-420°.

The speed of flow of the bromobenzene during the reaction is very important. If the speed is too low, much of the bromobenzene fails to react and the yields of phenylbromosilanes are low.

Table 6 illustrates the effect of flow velocity of the bromobenzene on the yield of phenylbromosilanes.

TABLE 6

Effect of Flow Rate of Bromobenzene on the Reaction Yield at 420-430°

No. of preparation	C_6H_5Br passed through (g)	Duration of experiments (hours)	Weight of reaction products (g)	Amount of organosilicon compounds	
				(in g)	(in %)
1	276	20	260.0	131.3	50.5
2	450	24	434.0	184.0	42.5

In the preparation of phenylbromosilanes, just as in that of methylbromosilanes, the reaction velocity increases in the first 10-12 hours after the start of a given series of experiments and then gradually decreases due to consumption of the silicon (Table 7).

TABLE 7

Course of Formation of Phenylbromosilanes with Passage of Time at Various Temperatures

No. of preparation	410-420°			440-460°		
	Duration of experiments (hours)	Consumption of bromobenzene (g)	Amount of organosilicon compounds formed (g)	Duration of experiments (hours)	Consumption of bromobenzene (g)	Amount of organosilicon compounds formed (g)
1	6	75	31	6	75	30.4
2	6	75	53	6	75	69
3	6	75	45.7	6	75	54
4	6	75	44	6	75	40
5	6	75	38	6	75	37
6	6	75	30	6	75	30
7	6	75	25	6	75	28
Total . .	42	525	266.7	42	525	288.4

Composition of Products of Reaction of Bromobenzene with Silicon in Presence of a Catalyst (Copper)

The composition of the products was investigated by subjecting the mixture to fractionation.

Table 8 gives details of the fractionation of mixtures of phenylbromosilanes prepared by direct synthesis at various temperatures.

We established that the obtained wide-range fractions are technical products with essentially the following compositions: First fraction — unreacted bromobenzene and silicon tetrabromide; second fraction — phenyltribromosilane, not previously described in the literature; third fraction — intermediate; fourth fraction — diphenyldibromosilane; the residue at above 200° at 12 mm contained a small amount of triphenylbromosilane.

For the purpose of isolation of the individual phenylbromosilanes the prepared fractions (Table 8) were cut at 12 mm into narrower fractions which were then tested for constancy of composition. We determined the bromine content of the phenylbromosilanes by two methods which checked each other: Alkali saponification and the Volhard method.

Table 9 gives the yields of silicon tetrabromide and of phenylbromosilanes at various experimental temperatures.

We see from Table 9 that with rising temperature the yields of phenyltribromosilane and silicon tetrabromide increase but the yield of diphenyldibromosilane decreases.

TABLE 8

Fractionation of Mixtures of Phenylbromosilanes Prepared by Direct Synthesis at Various Temperatures (Yield of Fractions Expressed as % of Material Charged)

No. of preparation	Fractions obtained	Experimental temperatures				
		400-410°	410-420°	420-430°	440-460°	480-500°
1	Up to 160° (760 mm)	59.47	50.7	54.7	57.2	56.57
2	110-150° (12 mm)	13.4	24.0	23.6	22.0	22.8
3	150-175° (12 mm)	6.86	2.62	6.15	2.7	6.3
4	175-200° (12 mm)	13.3	15.5	8.3	7.85	5.15
5	Residue above 200°	4.87	6.94	4.23	9.05	5.7
	Losses	2.1	0.24	3.02	1.2	3.48

TABLE 9

Yields of Phenylbromosilanes and Silicon Tetrabromide at Various Experimental Temperatures

No. of preparation	Experimental temperatures	$SiBr_4$	$C_6H_5SiBr_3$	Intermediate fraction	$(C_6H_5)_2SiBr_2$	Residue
1	400-410°	14.4	32.8	14.5	28.0	10.3
2	410-420	13.5	42.4	4.5	27.4	12.2
3	420-430	16.2	46.8	12.2	16.4	8.4
4	440-460	17.1	44.0	5.4	15.6	17.9
5	480-500	17.4	47.2	13.0	10.6	11.8

We were unable to isolate silicon tetrabromide ($SiBr_4$) in the pure state due to the closeness of its boiling point (154°) to that of bromobenzene (157°).

The amount of silicon tetrabromide obtained was determined by hydrolyzing the fraction which came over up to 160°; the bromobenzene was then removed by steam-distillation. At experimental temperatures of 400-500° we obtained 14-17% silicon tetrabromide (Table 9).

Phenyltribromosilane $C_6H_5SiBr_3$. This compound has not previously been described in the literature. Its isolation in the pure form was effected by subjecting the 110-150° (12 mm) fraction to repeated vacuum fractionation into narrower cuts, each of which was analyzed for the bromine content. The fraction with b. p. 130-131° at 12 mm had a bromine content closest to that of phenyltribromosilane.

The bromine was determined by saponification with alkali. 0.3779 g substance: 19.6 ml 0.5 N KOH; 13.21 ml 0.5 N H_2SO_4 0.4323 g substance: 19.6 ml 0.5 N KOH; 12.24 ml 0.5 N H_2SO_4. Found %: Br 68.27, 68.80. $C_6H_5SiBr_3$. Calculated %: Br 69.58.

Volhard determinations of the bromine invariably gave slightly lower results; the cause of this was the resinous precipitate, formed when the sample was introduced into silver nitrite solution, which evidently adsorbed some of the bromine.

A resin is also precipitated during determination of bromine in phenyltribromosilane by alkali saponification, but since the sample is refluxed with the alkali solution for 1½ hours the analysis is more accurate.

Diphenyldibromosilane $(C_6H_5)_2SiBr_2$. The fraction with b.p. 175-200° at 12 mm, obtained by fractionation of the crude mixture of phenylbromosilanes, was cut at 12 mm into narrow fractions whose bromine contents were determined.

The bromine content of the 190-194° (12 mm) cut closely approached that of diphenyldibromosilane. This fraction solidified at −70°.

0.2474 g substance: 14.82 ml 0.1 N $AgNO_3$. 0.2460 g substance: 14.88 ml 0.1 N $AgNO_3$ (Volhard). 0.3316 g substance: 4.45 ml 0.5 N KOH. 0.3822 g substance: 4.55 ml 0.5 N KOH (saponification). Found %: Br 46.11, 46.56, 46.64, 47. $C_{12}H_{10}SiBr_2$. Calculated %: Br 46.78.

The identity of this fraction, b.p. 190-194°, with pure diphenyldibromosilane was confirmed by the purity of the diphenylsilanediol which we obtained by hydrolyzing the fraction.

Triphenylbromosilane $(C_6H_5)_3SiBr$. The residue, which boiled at above 200° at 12 mm, was fractionated at 3 mm; between 200 and 220° a colorless crystalline substance came over, m.p. 114-118° (according to the literature $(C_6H_5)_3SiBr$ melts at 118-120°). The bromine content of these crystals (using the saponification method) was 26-27% Br (mean value) (calculated for $(C_6H_5)_3SiBr$ 23.6%). The slightly high bromine content and the slightly

low melting point are explained by the lack of purity of the substance. We were unable to recrystallize the triphenylbromosilane because the quantity was insufficient.

In the temperature range of 250-300° (3 mm) we obtained a viscous, red liquid with a mean bromine content of 49%.

General properties of the phenylbromosilanes. Phenylbromosilane and diphenyldibromosilane are heavy, colorless liquids; triphenylbromosilane is a colorless, crystalline substance. All the phenylbromosilanes fume in the air and are readily hydrolyzed by water; they distill in vacuum without decomposition.

SUMMARY

A direct synthesis of methyl- and phenylbromosilanes was effected and the composition of the distilled fractions was investigated.

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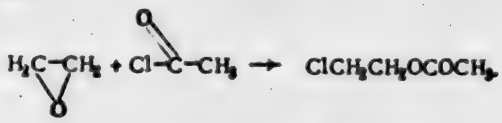
OLEFIN OXIDES

IX. CONDENSATION OF OLEFIN OXIDES WITH NITROSYL CHLORIDE

M. S. Malinovsky and N. M. Medyantseva

We know that olefin oxides react with organic acids to form glycol monoethers, while replacement of the acid by the anhydride leads to diethers. These reactions are well-known [1,2,3] and are exploited on the industrial scale for the production of certain ethers utilized as solvents.

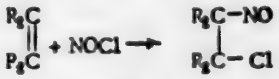
Much less study has been devoted to the reaction between olefin oxides and acid chlorides which, generally speaking, ought to present interest in view of the synthesis of halo-substituted esters containing halogens in the alcohol radical, for example:



Still more neglected have been the reactions of oxides with chlorides of inorganic acids, although the resultant products may be utilized as starting materials for further syntheses.

With the aim of filling this gap, we investigated the action of nitrosyl chloride and carbonyl chloride on the oxides of ethylene, propylene and cyclohexene, and on epichlorhydrin. We report the results in this communication.

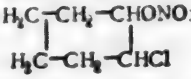
Reactions between nitrosyl chloride and organic compounds may proceed in two directions. First, the whole of the nitrosyl chloride adds on to the substance with which it reacts, undergoing preliminary splitting into NO and chlorine. Double-bond compounds thus usually react with it as follows:



This form of reaction has been closely investigated by N. Ya. Demyanov [2] and pupils.

Second, the nitrosyl chloride simultaneously oxidizes, chlorinates and nitrites the substance. Benzaldehyde is transformed into benzoyl chloride and benzoic acid, while ethyl, isopropyl and butyl alcohols give the corresponding nitrites [5]. Secondary amines react with nitrosyl chloride to form nitrosamines [6]; acetone yields isonitrosoacetone [7], and so on.

Nitrosyl chloride will obviously react with olefinoxides in one of these directions, and most probably in the first; this prediction has been fully confirmed by experiment.

We obtained the following chloralkyl nitrites: From ethylene oxide $ClCH_2CH_2ONO$; from propylene oxide $ClCH_2CH(ONO)CH_3$, from cyclohexene oxide  ; from epichlorhydrin $ClCH_2CH(ONO)CH_2Cl$.

The structure of the reaction products was confirmed by saponification which gave the corresponding glycol chlorhydrins; the latter were identified as such and also transformed into the α-oxides. Furthermore, some of these esters are described in the literature (they had been prepared by other methods) and their constants agreed fully with those in the literature.

The esters prepared from olefin oxides and nitrosyl chloride possess a characteristic odor which causes headaches.

EXPERIMENTAL

Nitrosyl chloride was prepared from nitrosylsulfuric acid and sodium chloride [8]. Condensation with the oxides was effected in a medium of ether (equal volumes). In these conditions the sole product of condensation is the corresponding ester of nitrous acid, which is formed in good yield. In the absence of ether as a diluent, the

yield of nitrous acid ester is considerably reduced due to formation (in many cases) of a certain oily substance containing nitrogen, which does not distill in vacuum and on keeping rapidly decomposes with separation of oxalic ac (when using ethylene oxide and propylene).

1) Condensation of ethylene oxide with nitrosyl chloride. Ethylene oxide (10 g) was diluted with an equal volume of anhydrous ether, and through this mixture (cooled) was passed a stream of nitrosyl chloride until the liquid had acquired a slightly reddish color, which indicated a slight excess of nitrosyl chloride (in the absence of this excess a good deal of the oxide remains unchanged). The mixture was then stood in iced water for 24 hours, following which it was subjected to fractionation. If the mixture had not been allowed to stand for the specified period and distilled quickly or after standing for 2 hours, then a condensation product could not usually be isolated. The oxide and nitrosyl chloride then distill over unchanged.

After distilling off the ether on the water bath from the product which was allowed to stand for 24 hours, the residue was distilled from a small flask with a dephlegmator. A total of 18 g colorless liquid was obtained with b.p. 94-95° at 730 mm (after a second distillation). The yield was 72.5% of the theoretical. Specific gravity 1.2178 (at 20°).

0.2254 g substance: 0.2915 g AgCl. Found %: Cl 32.04. $C_2H_4O_2NCl$. Calculated %: Cl 32.42.

Ethylene chloronitrite had originally been prepared by the action of hydrochloric acid on an aqueous solution of equimolar amounts of ethylene chlorohydrin and sodium nitrite [9] The constants reported for it in the literature are: b.p. 95-96° at 764 mm; d_4^{20} 1.221.

Heating of the ethylene chloronitrite prepared by us with a solution of sodium hydroxide caused ethylene oxide to separate, and sodium nitrite was detected in the solution.

2) Condensation of propylene oxide with nitrosyl chloride. The condensation was performed as above. After the mixture had stood for 24 hours, the ether was distilled off together with unreacted propylene oxide, and the residue fractionally distilled from a flask with a dephlegmator. 11.8 g of liquid was obtained (from 7 g oxide) with b.p. 101-102° at 730 mm, d_4^{20} 1.1214, which fully agreed with the literature data for this compound [9]. The prepared nitrous ester was saponified with potassium carbonate solution to give propylene chlorohydrin with the composition $CH_3CH(OH)CH_2Cl$ (b.p. 128-130°, in agreement with the literature), which confirms the above formul for the nitrous ester.

0.2197 g substance: 0.2573 g AgCl. Found %: Cl 28.90. $C_3H_6O_2NCl$. Calculated %: Cl 28.70.

3) Condensation of cyclohexene oxide with nitrosyl chloride. 7 g cyclohexene oxide (b.p. 129-130°) was condensed with nitrosyl chloride as in the preceding experiments. There was obtained 8 g faintly yellow, oily liquid with b.p. 81-83° at 23 mm, d_4^{20} 1.1468. Yield 64% of the theoretical.

0.2054 g substance: 0.1742 g AgCl. Found %: Cl 21.39. $C_6H_{10}O_2NCl$. Calculated %: Cl 21.70.

Treatment with potassium carbonate solution converted the substance into cyclohexene chlorohydrin; heating with caustic alkali solution led to reformation of cyclohexene oxide, thereby confirming the above formula

4) Condensation of epichlorohydrin with nitrosyl chloride. Condensation was performed with 7 g epichlorohydrin and 9 g $ClCH_2CH(ONO)CH_2Cl$ was obtained or 76% of theory.

The synthesized ester was a colorless liquid with b.p. 72-74° at 42 mm, d^0 1.3434. Careful saponification with weak potassium carbonate solution resulted in formation of $ClCH_2CH(OH)CH_2Cl$, while treatment with caustic alkali gave epichlorohydrin.

0.1974 g substance: 0.3514 g AgCl. Found %: Cl 44.80. $C_3H_5O_2NCl_2$. Calculated %: Cl 44.90.

SUMMARY

1. The reaction between olefin oxides and nitrosyl chloride, which permits the preparation of chloroalkyl nitrites in good yield, was studied.

2. Two new chloroalkyl nitrites were synthesized for the first time.

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Laboratory Organic Chemistry,
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SUGAR DERIVATIVES OF AMINO ACIDS

I. QUINOVOSYL-GLYCINE AND ITS DERIVATIVES

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Carbohydrate-amino acid compounds, which can be regarded as the simplest representatives of the carbohydrate-peptide and carbohydrate-protein complexes, play an important part in biochemical processes and present great interest for biochemistry, biology and chemotherapy.

Carbohydrate-protein complexes enter into the composition of antigens and toxins of microorganisms [1,2]. The specific polysaccharides isolated from microorganisms [2, 3, 4] and also found in higher organisms [5] are carbohydrate-amino acid (peptidic) and monose complexes.

V. G. Drobotko [6], Sh. D. Mashkovsky [7] and others draw attention to the possibility of utilization as medicinal preparations of amino acid analogs, examples of which are synthetic carbohydrate derivatives of amino acids.

In 1949 A. I. Oparin and D. N. Bezinger [8] isolated a high-molecular compound from champagne by dialysis and precipitation with alcohol. Hydrolysis of this compound gave a carbohydrate and a peptide. In the authors' opinion complex compounds are formed in natural wines from amino acids or peptides and sugars with participation of yeasts and their autolyzates. They consider that "these compounds can be extremely diverse in structure, size of complex and bond stability, and their investigation is of undoubted interest for biochemistry because of the demonstrated close connection between these complexes and metabolism."

V. Kretovich and R. Tokareva [9], showed that sugars react with amino acids in various fermentation processes.

Attention was drawn for the first time to the possibility of reaction between sugars and amino acids by the Russian workers S. Kostychev and V. Brilliant [10]. They showed [11] that sugars containing a free reducing group are capable of forming compounds with amino acids and peptides whose carboxyl group permits the formation with copper hydroxide of insoluble precipitates [12]. The carbohydrate-amino acid complexes of S. Kostychev and V. Brilliant are labile and decompose to give the original components. The work of these investigators was continued by N. Ivanov [13].

The work of these and many other investigators made it clear that the reaction of amino acids with sugars involves the amino group of the amino acid and the carbonyl group of the sugar. Further work in this field has been directed toward the synthesis of this type of product.

A. M. Kuzin and O. I. Polyakova [1] prepared a glucoside of glycine in the form of the calcium and barium salts. J. C. Irvine [14] synthesized a glucoside of alanine, and A. Stepanov and V. Mameva [15] obtained β-glucosyl-N-lysine.

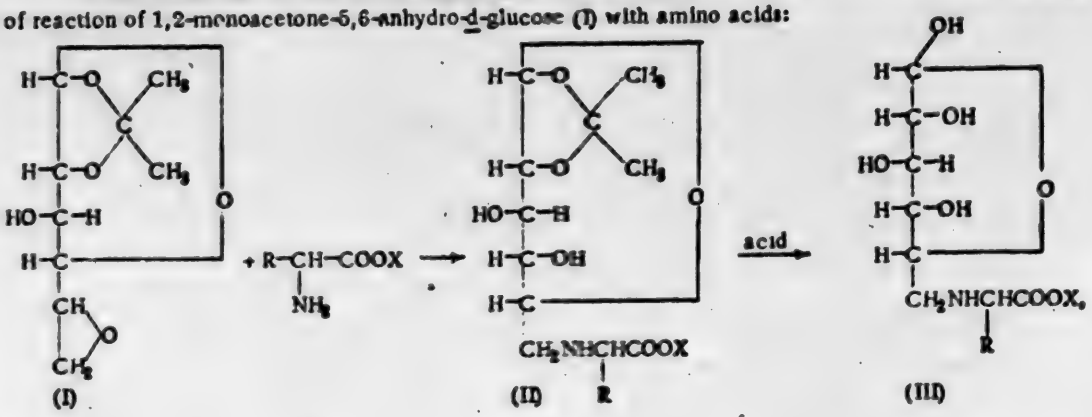
Some amino acids and peptides have been brought into reaction with glucose or with halogen-containing hexoses and bioses in the form of their ethyl esters [16]. The compounds prepared in this way decompose when saponified [17].

Study of the modes of reaction of carbohydrates with proteins is complex; it is naturally necessary at the start to study the possible modes of interaction of carbohydrates with the simple breakdown products of proteins — amino acids.

The presence in both amino acids and monoses of several functional groups makes possible a whole variety of reactions between them. The hydroxyl group of the sugar might be esterified by the carboxyl group of the amino acid; a link-up may occur through the hydroxyl group of the monose and the hydroxyl (or SH) group of hydroxy-amino acids of the type of serine (or cysteine); glucosides of simple sugars may be formed at the cost of the NH_2-, OH- or SH- group of amino acids; finally, those saccchariferous amino acids in which the amino group belongs

simultaneously to an amino sugar and an amino acid constitute a special group of substances [18]. The possible diversity of these compounds is evident from the fact that one molecule of a monose can be linked with several identical or different amino acids.

We set ourselves the task of investigating the unusual group of sugar derivatives constituting the products of reaction of 1,2-monoacetone-5,6-anhydro-d-glucose (I) with amino acids:



where R is a radical and X is hydrogen, barium or alkyl.

Consequently we obtain carbohydrate-amino acid compounds which can be regarded as a new group of the simplest representatives of the carbohydrate-peptide and carbohydrate-protein complexes, distinguished by having the nitrogen atom linked with the sixth and not with the first carbon atoms of the monose.

I. Methods of condensation of monoacetone-anhydroglucose with amino acids. The synthesis of the only 6-amino acid derivative of glucose reported in the literature, 6-(N-alanine)-glucose, was described as far back as 1938 by Helferich and Mittag [19], but the problem has not aroused interest since then. The authors condensed anhydroglucose with the ethyl ester of alanine at room temperature, saponified the ester group and the acetone residue, and so obtained 6-(alanine)-glucose in 10% yield.

Utilizing this method we obtained products of condensation of monoacetone-anhydroglucose with the methyl ester of tyrosine, the ethyl ester of p-aminobenzoic acid and the butyl ester of glycine. The method proved to be simple in application, the reaction proceeds in solution and in a melt, and in the presence or absence of pyridine (catalyst). In some cases (cystine), however, the esters of the amino acids are converted during the reaction almost completely into the corresponding derivatives of diketopiperazine and other more complex products [20].

We therefore attempted to carry out the condensation of the anhydroglucose with amino acids, utilizing the observation of A.I. Kiprianov and other workers [21] that aliphatic amino acids are capable of reacting with organic α-oxides. Experiments were performed in melts and in solution, also in presence of a catalyst, but no reaction occurred. Evidently the peculiar structure of this organic oxide here plays a part.

We then developed a new and more convenient method of preparation of sugar derivatives of amino acids, consisting in replacing the free amino acids in the reaction with 1,2-monoacetone-5,6-anhydro-d-glucose by their barium salts, which are usually readily soluble in water and can be prepared by dissolving the amino acids in 0.1-0.2 N barium hydroxide. This method permitted us to prepare monoacetone-quinovose derivatives of various amino acids. Reaction of one mole of the barium salt of an amino acid with two moles of the anhydroglucose gives the bis-(monoacetone-quinovosyl)-N-amino acid.

The pH of the medium is exceptionally important for a successful outcome of the reaction. There are indications that many reactions involving addition to anhydroglucose proceed only in a weakly alkaline medium. Thus, for example, the addition of hydrogen sulfide to anhydroglucose takes place in barium hydroxide solution, and the preparation of 6-alkyl [22] and 6-aryl ethers of monoacetone-glucose [23] is only possible in presence of an alcoholate or phenolate.

Moreover, as shown by G. Lampson and co-workers [24], anhydroglucose reacts readily with disodium phosphate (pH of solution 9.7), whereas no reaction occurs with mono- and trisodium phosphates, due to the strong acidity or alkalinity of the media. The pH of solutions of barium salts is within the range of 8-10, thus being comparable to that of disodium phosphate.

No report has hitherto appeared in the literature on the performance of the reaction between salts of amino acids and organic oxides; we therefore now describe our method: 1-1.2 equivalents of the free amino acid are dissolved in a standard solution of barium hydroxide (0.05-0.2N); solution of the amino acids which we investigated took place in the cold. The solution has an alkaline reaction, due to hydrolysis. Alkalinity is detrimental to the anhydroglucose and is prevented by taking 0.01-0.05 equivalents of barium hydroxide less than is required by calculation.

Addition is made to the solution of the barium salt of the amino acid of 1 equivalent of anhydroglucose which rapidly goes into solution. Flask and contents are immersed in a boiling water bath and refluxed for 1-3½ hours. The solution remains transparent and colorless. At the end of the stated period, addition is made to the hot solution of the calculated amount of 0.4 N sulfuric acid solution in order to remove the barium. The flask contents are shaken for a short period by hand or on a machine until all the carbonate has been converted into barium sulfate. After cooling slowly, the solution filters without special difficulty. The filtrate is tested for freedom from barium, evaporated to dryness in vacuum at a bath temperature not higher than 50-60°, and the product is dried toward the end in a vacuum at 90-95°.

The residue in the flask is the crude product of condensation of the anhydroglucose with amino acids and is often amorphous. The purification procedure will vary with the properties of the amino acid in each particular case. By this method we succeeded in preparing sugar derivatives of such sparingly water-soluble amino acids as tyrosine (1 part dissolves in 2400 parts water) and cystine (1 in 1840 water). In these cases it was necessary to resort to high dilutions of the solution due to the poor solubility of their barium salts.

Bis-monoacetone-quinovosyl derivatives of diamino acids were prepared by reacting two moles of the anhydroglucose with one mole of amino acid.

This method is entirely suitable for preparation of products of condensation of anhydroglucose with di- and polypeptides; for these, however, we must use 0.05 N barium hydroxide solution for dissolving the peptide in order to avoid hydrolysis of the peptide bond.

The applicability of this method is not limited to the reactions of anhydroglucose with amino acids; it can be recommended for preparation of derivatives of amino acids with those organic α-oxides which do not undergo hydration in aqueous solution in the course of 3-4 hours. We succeeded, for example, in effecting the reaction between the cystine salt and ethylene oxide, which yielded dihydroxyethyl cystine.

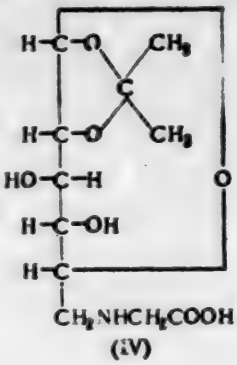
Concerning the cleavage of the acetone residue from monoacetone-quinovosyl-amino acids, this can be effected with the following acids (according to the literature): 0.05-0.1 N sulfuric, hydrochloric, nitric, and acetic acid (in various concentrations from 35% to glacial). The duration and temperature of the reaction vary within very wide limits. After testing the majority of these methods both in the cold and on the water bath, we arrived at the conclusion that all these methods, in their original form, are unsuitable for the present problem. Hydrolysis with 0.1 N sulfuric acid or with acetic acid in the cold or with heating is observed to cause very drastic saponification of the hydrolsis product, and purification is made difficult. We developed a new method of hydrolysis of monoacetone-quinovosyl-amino acids, based on utilization of a hydrogen atmosphere.

The product of condensation of anhydroglucose with the amino acid is dissolved in 5-10-50 times the volume of 50% acetic acid in a flask fitted with a reflux condenser and a tube reaching to the bottom through which hydrogen is bubbled. Hydrogen is first passed through for a few minutes in order to drive out the air from the flask. The flask is thereupon immersed in a boiling water bath while hydrogen is bubbled steadily for 3-4 hours. During the first 2½ hours the solution remains colorless, but by the end of the heating period the color is faint yellow. The contents are then decolorized with a small quantity of active carbon. The filtrate is evaporated in a vacuum at a bath temperature of 50-60°. After the whole of the liquid has evaporated, addition is made to the flask through the dropping funnel of a few ml distilled water and evaporation is repeated. This operation is repeated 3-4 times until all the acetic acid has been removed. Decolorization with active carbon is repeated at this stage, if necessary, and the liquid is filtered and evaporated in vacuum. The procedure for further purification of the hydrolysis product will vary with the individual case, depending on the solubility and other properties of the prepared substance. This method permitted the cleavage of the acetone residue from the majority of our products of condensation of anhydroglucose with amino acids.

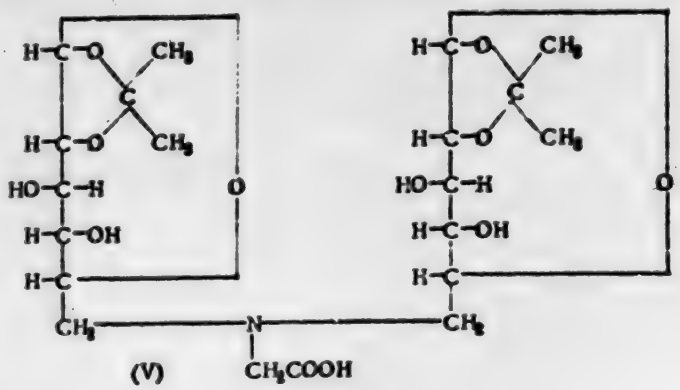
II. Condensation of anhydroglucose with the barium salt of glycine. Reaction between 1,2-monoacetone-5,6-anhydroglucose (I) and amino acids leads to a compound of type (II), cleavage from which of the acetone

residue yields a compound of type (III). The name d-quinovosyl -6- has been assigned in the literature to the glucose residue obtained after removal of hydroxyl from the sixth carbon atom; hence compounds (II) and (III) can respe tively be named: 1,2-monoacetone-quinovosyl-6-N-amino acid and quinovosyl-6-N-amino acid.

We have prepared monoacetone-quinovosyl-6-N-glycine (IV) and bis-(monoacetone-quinovosyl-6,6')-N-glycine (V):



(IV)

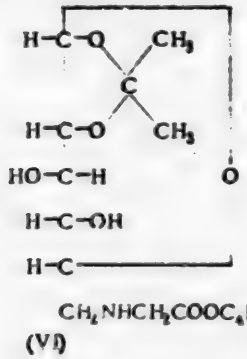


(V)

Substance (IV) was obtained in the crystalline form but (V) was amorphous. Their aqueous solutions are acid to litmus.

It has been reported [23] that 6-substituted esters of monoacetone-glucose are formed when carboxylic acids are heated with anhydroglucose to 140°. Esters with acetic and benzoic acids were thus prepared. It would thus be expected that also in the condensation of anhydroglucose with amino acids the amino acid residue would combine at the carboxyl group. We performed the condensation of anhydroglucose with the butyl ester of glycine for the purpose of demonstrating that our reaction between anhydroglucose and the barium salts of amino acids does not involve addition of the amino acid residue to the carboxyl group attached to the ethylene oxide ring.

In our case the addition indisputably takes place at the amino group, since the carboxyl group is esterified. The obtained compound (VI) gives, on saponificationwith barium hydroxide, a small yield of product (IV).



(VI)

Compound (IV), prepared by condensation of anhydroglucose with the barium salt of glycine, and the substance synthesized with the help of the butyl ester of glycine proved to be identical (in melting point, nitrogen content, specific rotation and chemical properties). Hence by using the barium salts of amino acids for the reaction with anhydroglucose we have the possibility of preparing compounds of the type of (IV) and (V).

After cleavage of the acetone residue from compounds (IV) and (V), quinovosyl-6-N-glycine and diquinovosyl 6,6'-N-glycine are isolated.

Both compounds are dextrorotary, whereas their 1,2-monoacetone derivatives are levorotatory. Their aqueous solutions do not undergo mutarotation. These glycine derivatives are readily oxidized in an acid solution even with atmospheric oxygen. They are probably decomposed into their components. Glucose gives rise to 5-hydroxymethylfurfural, which with amino acids gives colored products whose amount is smaller in a solution of diquinovosyl-amino acids.

In this respect there is full agreement with the data of M. Wolfrom [25] who observed that heating of amino acids with glucose in acid solution gave an amount of colored substances smaller than in the case of N-disubstituted amino acids.

EXPERIMENTAL

Reaction of Anhydroglucose with Glycine

1. a) Condensation of the anhydroglucose with barium salt of glycine. The monoacetone-glucose required for the investigation was prepared by the procedure of Zervas and Sessler [26] as modified by Gluzman and Litvinenko [27]. 6-p-Tosyl-monoacetone-glucose was prepared by A. Meyer's method [28] and then the anhydroglucose by the method of Ohle and Varga [29]. In the last two stages dichloroethane was substituted for chloroform without fall in yields.

1.1 g (14.6 millimoles) glycine is dissolved, by heating on the water bath, in 67.8 ml 0.2 N barium hydroxide. To the solution is added 2.78 g (13.6 millimoles) anhydroglucose. Further treatment is as described in the general account of the method above. After heating for 2½ hours the barium is precipitated with sulfuric acid (36.1 ml), and the residue after evaporation in vacuum and drying at 90-100° is digested with 10-15 ml dry ethyl acetate and then with acetone; the product is filtered and the residue on the filter is washed with acetone and dry ether. Yield 2.48 g (85% of the theoretical). The substance melts at 173-174° without decomposition. The aqueous solution of the prepared glycine derivative has an acid reaction; it readily dissolves barium carbonate and the barium can only be precipitated from it with sulfuric acid, and not with carbon dioxide.

$[\alpha]_D^{22}$ −6.3° (c = 2.922; water).

0.1467 g substance: 5.17 ml 0.1 N H_2SO_4. 0.1659 g substance: 5.90 ml 0.1 N H_2SO_4. Found %: N 4.93, 4.98. $C_{11}H_{19}O_7N$. Calculated %: N 5.04.

The prepared 1.2-monoacetone-quinovosyl-6-N-glycine is readily soluble in water and in dilute and glacial acetic acid; it is less soluble in the cold in 70% alcohol but readily dissolves when heated. The product is insoluble in dry acetone, ethyl acetate, benzene and dichloroethane. A white silver salt can be got from the aqueous solution by the usual method.

b) Hydrolysis of 1.2-monoacetone-quinovosyl-6-N-glycine. 2 g condensation product is hydrolyzed with 50 ml 50% acetic acid in a hydrogen atmosphere for 3 hours by the above-described method. The residue in the flask (1.2 g) is evaporated down and recrystallized from 50 ml absolute alcohol, and the crystals are washed with absolute methanol and dry ether. Yield 0.5 g (29% of the theoretical); m.p. 133-135°. Quinovosyl-6-N-glycine is soluble in water, dilute and glacial acetic acid, and methanol; it is insoluble in benzene, ether and dichloroethane; it readily reduces Fehling solution when heated on the boiling water bath.

$[\alpha]_D^{22}$ +30.8° (c = 0.973, water).

0.1534 g substance: 6.24 ml 0.1 N H_2SO_4. 0.1408 g substance: 5.78 ml 0.1 N H_2SO_4. Found %: N 5.69, 5.74. $C_8O_{15}H_7N$. Calculated %: 5.90.

Quinovosyl-6-N-glycine was characterized by the preparation of its phenylosazone. 0.1 g of the substance and 0.2 g phenylhydrazine are dissolved in 5 ml water and 0.3 ml 50% acetic acid. The solution is heated on the water bath for 1 hour. Toward the close of the heating a brownish substance forms on the walls of the vessel. The solution is allowed to stand overnight, the crystals are filtered and washed with 10% acetic acid, water, toluene and ether. Yield 0.07 g. M.p. of the phenylosazone 149°.

2. a) Condensation of 2 moles anhydroglucose with the barium salt of glycine. 0.39 g (5.2 millimoles) glycine is dissolved by heating in 24 ml 0.2 N barium hydroxide. To the solution is added 2.1 g (10.3 millimoles) anhydroglucose, heating for 2½ hours. The barium is precipitated with 12.2 ml 0.4 N sulfuric acid. Further treatment is as in the previous case. The residue in the flask is digested with ethyl acetate and then with acetone (20 ml) filtered, washed with dry ether and dried in vacuum. M.p. 168-169°. Yield 1.25 g (50.2% of the theoretical).

$[\alpha]_D^{18}$ −8.2° (c = 1.439; water).

0.2134 g substance: 4.09 ml 0.1 N H_2SO_4. 0.1588 g substance 3.25 ml 0.1 N H_2SO_4. Found %: N 2.68, 2.87. $C_{20}H_{33}O_{12}N$. Calculated %: N 2.92.

The prepared bis-(monoacetone-quinovosyl-6,6')-N-glycine is readily soluble in water and in aqueous and glacial acetic acid. The aqueous solution is acid to litmus and dissolves barium carbonate. The compound does not reduce Fehling solution.

b) Hydrolysis of bis-(monoacetone-quinovosyl-6,6')-N-glycine. 1.5 g of the compound is dissolved by heating for 3 hours with 38 ml 50% acetic acid in a hydrogen atmosphere; further treatment as for the monosubstituted glycine. Yield of crude product 0.75 g (59% of the theoretical). The substance is successively digested with 15 ml absolute ethanol and 12 ml absolute methanol; it is then washed on the filter with absolute methanol and dry ether. Yield 0.25 g (19.2% of the theoretical). An additional 0.2 g product is recovered from the combined alcoholic filtrates after decolorization with active carbon and evaporation at room temperature. The synthesized product decomposes at 110-120° and is a white substance readily soluble in water, 50% methanol, ethanol, isopropanol; poorly soluble in other organic solvents; it readily reduces Fehling solution when heated. It

also gives a positive reaction for a free carboxyl group (formation of salts). It does not form a color with an aqueous solution of ninhydrin.

$[\alpha]_D^{22}$ +23.8° (c = 0.911; water).

0.1840 g substance: 4.68 ml 0.1 N H_2SO_4. 0.1224 g substance: 3.03 ml 0.1 N H_2SO_4. Found %: N 3.56, 3.47. $C_{14}H_{25}O_{12}N$. Calculated %: N 3.50.

3. a) Condensation of 1,2-monoacetone-5,6-anhydro-d-glucose with the n-butyl ester of glycine. To a warm solution of 1.55 g (7.6 millimoles) anhydroglucose in 15 ml dry dichlorethane is added 1.6 g (12 millimoles) butyl ester of glycine prepared by Abderhalden's method [30]. The mixture is well stirred and heated to 60-70°. A pale yellow solution is formed which is allowed to stand for 3 days at room temperature.

At the expiration of this period the dichlorethane and excess butyl ester are distilled off at 3-4 mm at a bath temperature of 100°. The oil remaining in the flask is heated with 16 ml distilled water on a water bath for 3 hours under a reflux condenser. During this treatment the residual butyl ester of glycine is partly converted into diketopiperazine which dissolves in the water, while the glucose derivative remains in the form of a viscous oil. After separating the aqueous solution, the residue is worked up 6 times with 15-20 ml lots of chloroform. The combined chloroform extracts are decolorized with active carbon and dried with sodium sulfate prior to distillation of the solvent. The product is a faint-yellow, amorphous, very hygroscopic substance with a softening temperature of 50-60°; it is readily soluble in chloroform, acetic acid, and methanol, less readily soluble in dichlorethane and acetone. Water precipitates it from methanol solution as a viscous oil. Yield of n-butyl ester of 1,2-monoacetone-quinovosyl-6-N-glycine 2.3 g (90% of the theoretical).

$[\alpha]_D^{22}$ +14.6° (c = 1.732; dry chloroform).

0.1374 g substance: 3.92 ml 0.1 N H_2SO_4. 0.1968 g substance: 5.76 ml 0.1 N H_2SO_4. Found %: N 3.99, 4.10. $C_{15}H_{27}O_7N$. Calculated %: N 4.20.

The condensation of the anhydroglucose with the equivalent amount of butyl ester of glycine can be performed by heating the solution on the water bath. Formation of diketopiperazine cannot then be observed. The same results can be achieved by performing the condensation in a mixture of dichlorethane and dry methanol (8:1). Large amounts of methanol might result in formation of 1,2-monoacetone-6-methylglucose, which contaminates the main product.

b) Hydrolysis of the butyl ester of 1,2-monoacetone-quinovosyl-6-N-glycine. 2.5 g of the butyl ester is dissolved by heating in 200 ml 0.2 N barium hydroxide solution (3 equivalents). The solution is left at room temperature for 6 hours, after which the barium is precipitated with sulfuric acid. After evaporation in vacuum of the filtrate (following decolorization with active carbon), the residue is a colorless, amorphous, hygroscopic substance. The product of hydrolysis is dissolved in 10 ml dry acetone by heating and the solution seeded with the product of condensation of the anhydroglucose with glycine prepared via the barium salt of glycine. The acetone solution is left for 5-6 days, in the course of which crystals come down which are repeatedly triturated with 10 ml dry acetone. Yield of crystalline product 0.5 g (24% of the theoretical). Evaporation of the acetone filtrates leaves an amorphous substance with the same nitrogen content as the crystalline product. M.p. of the crystalline product 173-175° (without decomposition). The crystalline product did not depress the melting point of the product of condensation of the anhydroglucose with glycine (prepared via the barium salt).

$[\alpha]_D^{25}$ −7.8° (c = 2.29; water).

0.1750 g substance: 6.20 ml 0.1 N H_2SO_4. 0.1860 g substance: 6.76 ml 0.1 N H_2SO_4. Found %: N 4.96, 5.08 $C_{14}H_{25}O_7N$. Calculated %: N 5.04.

The aqueous solution of 1,2-monoacetone-quinovosyl-6-N-glycine, prepared via the butyl ester of glycine, has an acid reaction to litmus, which points to the presence of a free carboxyl group; it gradually dissolves barium carbonate.

SUMMARY

1. The literature on carbohydrate-protein and -peptide complexes is briefly surveyed and attention is drawn to the importance of these substances in biology, biochemistry and chemotherapy.

2. A new and convenient method is developed for the preparation of a group of sugar derivatives of amino

acids in which the sixth carbon atom of a monose is linked to the amino acid through the nitrogen atom of the amino group. The method involves condensation of monoacetone-anhydroglucose with barium salts of amino acids.

3. Monoquinovosyl-6- and diquinovosyl-6,3'-N-glycines and their acetone derivatives have been prepared, as well as the butyl ester of monoacetone-quinovosyl-6-N-glycine.

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N-BROMO(CHLORO)-N'-ARYLSULFONYL QUINONEDIIMINES

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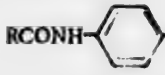
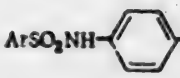
Some new substituted quinoneimines were described in previous papers, namely: quinonebromoimides and quinonedibromodiimides [1,2], quinonediiododiimides [3], N-arylsulfonyl quinoneimines [4], and N-arylsulfidyl quinoneimines [5].

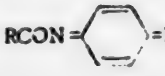
On the basis of the reaction of formation of quinonebromoimides and quinonedibromodiimides one of us has described a sensitive reaction for p-diamines, p-aminophenols and alkyl ethers of the latter [1,6]. Observations on the quinonebromoimide reaction have shown that N-acetyl(benzoyl)-1,4-phenylenediamine (Formula I) does not undergo the quinonebromimide reaction, whereas N-arylsulfonyl-1,4-phenylenediamine (Formula II)


(I)


(II)

exhibits an intense quinonebromoimine reaction. These facts prompted us to study the action of bromine and hypobromites on substituted p-phenylenediamines. It transpired that an alkaline solution of hypobromite acts on N-acetyl-1,4-phenylenediamine (Formula I; R = CH_3) to give a compound in the form of small yellow needles. Attempts to isolate the reaction product in the pure form were unsuccessful; the new compound rapidly changes in composition.

A more stable product is formed, however, by the action of hypobromite on N-arylsulfonyl-1,4-phenylenediamine. Evidently the absence of the quinonebromimide reaction with N-acetyl (benzoyl)-1,4-phenylenediamine and its occurrence with N-arylsulfonyl-1,4-phenylenediamine, as well as the great stability of the product of reaction with hypobromite, indicate that the oxidation potential of N-acetyl (benzoyl)-N'-bromo-1,4-benzoquinonediimine (Formula III)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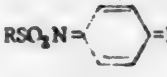
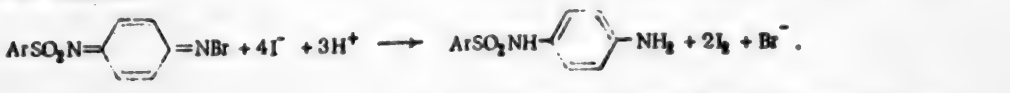

(IV)

is considerably higher than that of N-arylsulfonyl-N'-bromo-1,4-benzoquinonediimine (Formula IV).

A more convenient route to the latter compounds was found, however, in the action of bromine on a substituted phenylenediamine in acetic acid solution, followed by dilution with water. In this paper we describe the N-bromo-(chloro)-N'-arylsulfonyl-quinonediimines which have not previously been described in the literature.

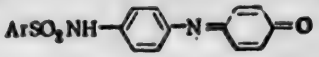
The synthesized N-bromo(chloro)-N'-arylsulfonyl-1,4-quinonediimines are crystalline substances with a yellow color. They differ from the quinone dibromodimides and quinonebromoimides in being fairly stable in the pure form at the ordinary temperature and in possessing sharp melting points. They decompose, usually with gas evolution, at a much higher temperature than their melting point. The N-bromo(chloro)-N-arylsulfonyl-quinonediimines, which we investigated, quantitatively liberate iodine from acidic solutions of iodides according to the equation:



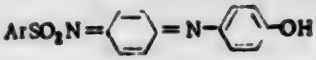
This reaction was utilized for determination of the oxidation equivalent of these compounds, and, consequently, for their identification.

In alkaline solution the new compounds readily react with phenols and very deep blue solutions are obtained from which dark-red indophenols separate on acidification. A qualitative test revealed the presence

of sulfur in these indophenols. Quantitative determination of sulfur indicates that the structure of the indophenols corresponds to formula (V) or (VI):



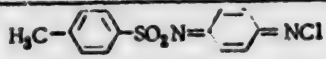
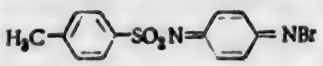
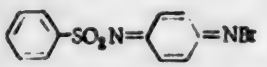
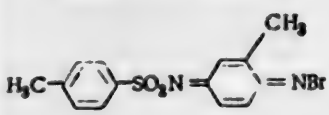
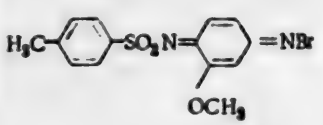
(V)



(VI)

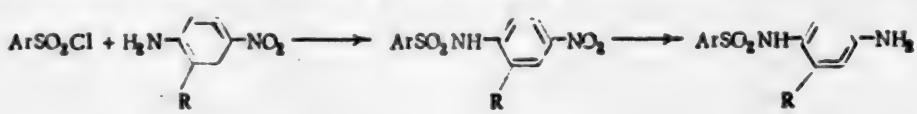
The prepared compounds are set forth in the table.

TABLE

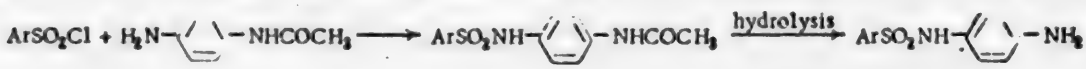
No.	Name	Formula	M.p.
1	N-Chloro-N'-p-toluenesul fonyl-1,4-benzoquinonediimine		93.1°
2	N-Bromo-N'-p-toluenesulfonyl-1,4-benzoquinonediimine		144.5
3	N-Bromo-N' benzenesulfonyl-1,4-benzoquinonediimine		132
4	N-Bromo-N^{4}-p-toluenesulfonyl-2,5-toluquinonediimine . .		47
5	N^{4}-Bromo-N^{1}-p-toluenesulfonyl-2-methoxy-1,4-benzo-quinonediimine		83.5

EXPERIMENTAL

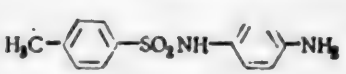
The N-arylsulfonated derivatives of 1,4-diamines required for synthesis of N-bromo(chloro)-N'-aryl-sulfonyl-quinonediimines were prepared in part according to the scheme:



In some cases it proved more convenient to proceed via the N-acetyl-1,4-diamines according to the scheme:



N-p-toluenesulfonyl-1,4-phenylenediamine



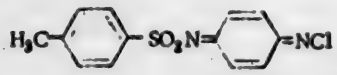
Preparation was by reduction of N-toluenesulfonyl-4-nitroanilide. The latter was synthesized by the action of toluenesulfochloride on 4-nitroaniline in acid solution. 55.2 g (0.4 mole) 4-nitroaniline was suspended in 200 ml xylene and 42.4 g calcined sodium carbonate (0.4 mole or a twofold excess) was added. The mixture was refluxed in a flask fitted with a stirrer and placed on a sand bath. p-Toluenesulfochloride (76.2 g; 0.4 mole) was added in portions to the boiling mixture. The completion of the reaction was indicated by disappearance of the reaction for 4-nitroaniline; this necessitated addition of an additional excess of toluenesulfochloride; heating was continued for 4 hours. The xylene was then distilled off with steam and the residue in the flask was extracted with 1 liter 3.5% sodium hydroxide solution. This effected separation from a by product, di-p-toluenesulfonyl-4-nitroanilide, which is insoluble in alkali. The alkali solution, after filtration from insoluble residue, was acidified with hydrochloric acid; the precipitate was filtered, washed with water and dried.

After washing with alcohol the precipitate had m.p. 189.3° (corrected, like all the other melting points.) After two recrystallizations the m.p. was 193°. The literature gives the m.p. of toluenesulfonyl-4-nitroanilide as 191° [7]. Yield 73.5 g, or 63% of the theoretical.

The nitro product was reduced with hydrosulfite in an alkaline medium. For this purpose, 73.0 g (0.25 mole) was dissolved in 1300 ml 3.5% NaOH, and at a temperature of 50-60° hydrosulfite was added until the reaction mass was decolorized. The filtered and cooled solution was then exactly neutralized with hydrochloric acid. The precipitate was filtered at the pump, washed with water, and dried. Yield 57.2 g 87.3% of the theoretical. M.p. 178.5° (unrecrystallized).

According to the literature [3] N-p-toluenesulfonyl-1,4-phenylenediamine melts at 186°.

N-Chloro-N'-p-toluenesulfonyl-1,4-benzoquinonediimine

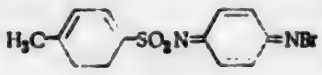


To 220 ml 0.2 N hypochlorite solution, prepared by passing chlorine gas into sodium hydroxide solution, was added at 0° (ice cooling) 4 g N-p-toluenesulfonyl-1,4-phenylenediamine in 25 ml 5% hydrochloric acid. The yellow precipitate was filtered and dissolved in dichloroethane. A portion of the dichloroethane was distilled off in vacuum and a small amount of ethyl alcohol was added to the residue. Small yellow needles crystallized out. M.p. (after drying in a vacuum desiccator) 93.1°. The yellow crystals are stable in ordinary conditions for several days. Readily soluble in ether, benzene and dichloroethane, poorly soluble in alcohol, soluble in water. In an ammoniacal medium it forms a deep-blue color with phenol and a blue-violet color with 1-naphthol.

The product was analyzed by determination of the oxidation equivalent. A weighed amount of the quinonediimine was dissolved in alcohol, an excess of KI solution was added and the mixture acidified with 10% H_2SO_4. The separated iodine was titrated with thiosulfate.

0.0624 g substance: 8.45 ml 0.1 N $Na_2S_2O_3$. 0.1000 g substance: 13.68 ml 0.1 N $Na_2S_2O_3$. Found: equiv. 73.94, 73.11. $\frac{1}{4}$ $C_{13}H_{11}O_2N_2ClS$. Calculated: equiv. 73.68. 0.1609 g substance: 0.1243 g $BaSO_4$ (Carius). Calculated %: S 10.63. $C_{13}H_{11}O_2N_2Cl_3$. Calculated %: S 10.68.

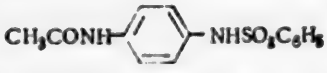
N-Bromo-N'-p-toluenesulfonyl-1,4-benzoquinonediimine



A solution of N-toluenesulfonyl-1,4-phenylenediamine in glacial acetic acid is added to a solution of bromine in glacial acetic acid, cooled to 0°. 3 moles bromine is taken for each mole of amine (i.e., a 50% excess). The mixture is carefully stirred and poured into cold water. The precipitate is filtered at the pump and washed with ethyl alcohol, prior to recrystallization from dichloroethane with addition of some gasoline. Dark yellow crystals, m.p. 144.5°. Less stable than the chloro derivative. Analysis shows presence of halogen and sulfur. Readily soluble in benzene, xylene and dichloroethane, difficultly soluble in alcohol. It rapidly decomposes in alkaline solutions. In an ammoniacal medium it gives a deep blue color with phenol and blue-violet with 1-naphthol. It was analyzed by determination of the oxidation equivalent (as detailed above).

0.0716 g substance: 8.50 ml 0.1 N $Na_2S_2O_3$. 0.0820 g substance: 9.72 ml 0.1 N. $Na_2S_2O_3$. Found: equiv. 84.29, 84.47. $\frac{1}{4}$ $C_{13}H_{11}O_2N_2BrS$. Calculated: equiv. 84.80.

N-Acetyl-N'-benzenesulfonyl-1,4-phenylenediamine



This compound is used for the preparation of N-benzenesulfonyl-1,4-phenylenediamine by the second scheme. It was synthesized by treating N-acetyl-1,4-phenylenediamine with benzenesulfochloride in presence of sodium carbonate in suspension in xylene. Reaction temperature 70°. After distilling off the xylene and extracting the unreacted N-acetyl-1,4-phenylenediamine with hot water, the product was crystallized from alcohol and melted at 157°. Pinkish needles. Yield 40 g (74.4% of the theoretical). Not described in the literature.

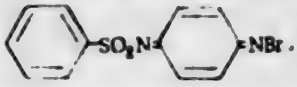
0.1484 g substance: 01197 g $BaSO_4$ (Carius). Found %: S 11.04. $C_{14}H_{14}O_3N_2S$. Calculated %: S 11.0

N-Benzenesulfonyl-1,4-phenylenediamine was prepared from the acetyl derivative by hydrolysis in alkalin solution. 40 g acetyl derivative (0.137 mole) was dissolved in 150 ml caustic alkali solution containing 12 g (0.3 mole) sodium hydroxide.

After heating for 6 hours on the water bath, the excess alkali was precisely neutralized with hydrochloric acid until the reaction to litmus was neutral. The white precipitate was recrystallized from alcohol. The obtained N-benzenesulfonyl-1,4-phenylenediamine has m.p. 170.5°.

The literature gives m.p. 173° [8]. Yield 20 g or 58.5% of the theoretical. It gives the quinonebromoimi reaction, procedure is described in [6].

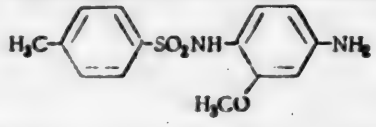
N-Bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine



The preparation was similar to that of the corresponding toluenesulfonyl derivative. Crystallization from dichloroethane with addition of alcohol gave dark yellow crystals with m.p. 132.0°. Sulfur and halogen are present. Readily soluble in benzene, xylene and dichloroethane. Gives a blue color with phenol in an ammoniacal medium and a violet one with 1-naphthol. It quantitatively liberates iodine from acidified solutions of iodides. Analysis was performed by determination of the oxidation equivalent by titrating the separated iodine with thiosulfate.

0.0605 g substance: 7.51 ml 0.1 N $Na_2S_2O_3$. 0.1032 g substance: 3.05 ml 0.1 N NaS_2O_3. Found: equiv. 80.67, 79.33. $\frac{1}{4}$ $C_{12}H_9O_2N_2BrS$. Calculated: equiv. 81.3. 0.1600 g substance: 0.1402 g $BaSO_4$ (Carius). Found %: S 9.56. $C_{12}H_9O_2N_2BrS$. Calculated %: S 9.81.

5-Amino-2-p-toluenesulfaminoanisole



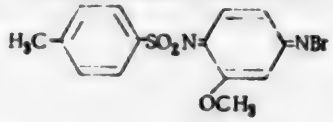
Prepared by reduction of 5-nitro-2-p-toluenesulfaminoanisole with hydrosulfite in an alkaline medium in a similar manner to the preparation of N-p-toluenesulfonyl-1,4-phenylenediamine. Reaction temperature 50-70°. A single crystallization gives colorless needles, m.p. 166°. Repeated crystallization raises the m.p. to 172.5°.

0.3000 g substance: 20.55 ml 0.1 N HCl (Kjeldahl). Found %: N 9.60. $C_{14}H_{16}O_3N_2S$. Calculated %: N 9.58.

In addition titration was performed with sodium nitrite (using the preparation with m.p. 166°).

0.3354 g substance: 11.6 ml 0.1 N $NaNO_2$. 0.4287 g substance: 15.0 ml 0.1 N $NaNO_2$. Found: equiv. 286.3, 286.2. $C_{14}H_{16}O_3N_2S$. Calculated: equiv. 292.3.

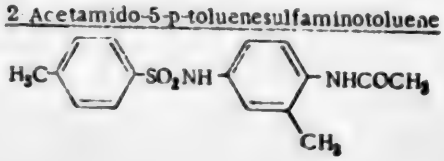
N⁴-Bromo-N¹-p-toluenesulfonyl-2-methoxy-1,4-benzoquinonediimine



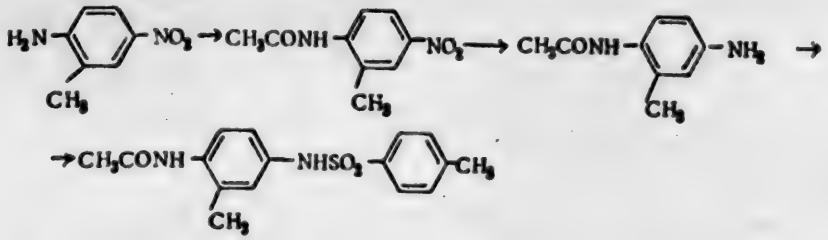
Prepared by the action of bromine on the preceding compound in solution in acetic acid. Crystallization from dichloroethane gave a yellow precipitate with m.p. 83.5°. It decomposes at 135° with charring and evolution of a red vapor. Readily soluble in organic solvents. Gives a blue (azure) color with phenol in an ammoniacal medium; with 1-naphthol the color is dark blue. The compound was analyzed by determination of the oxidation equivalent.

0.1220 g substance: 13.35 ml 0.1 N $Na_2S_2O_3$. 0.1182 g substance: 12.82 ml 0.1 N. $Na_2S_2O_3$. Found: equiv. 92.17, 91.58. $\frac{1}{4}$ $C_{14}H_{13}O_3N_2BrS$. Calculated: equiv. 92.28. 0.1602 g substance: 0.0966 g $BaSO_4$ (Carius). Found %: S 8.55. $C_{14}H_{13}O_3N_2BrS$ Calculated %: S. 8.69.

2-Acetamido-5-p-toluenesulfaminotoluene



The acetyl product necessary for preparation of the 2-amino-5-p-toluenesulfaminotoluene was prepared according to the following scheme:

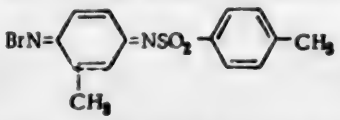


The procedure differed from that in the case of N-acetyl-N'-benzenesulfonyl-1,4-phenylenediamine in that the reaction was performed in aqueous solution. 10.6 g sodium carbonate (0.1 mole) was dissolved in 200 ml water and addition was made to the solution of 16.52 g (0.1 mole) 5-amino-2-acetylaminotoluene. The mixture was heated to 70° in a flask on a water bath fitted with a stirrer and a reflux condenser. With energetic stirring at the specified temperature addition was made in small portions of 19 g (0.1 mole) p-toluenesulfochloride. After 4 hours the precipitate was filtered, washed with water and recrystallized from alcohol. Light pink needlets, m.p. 166°. Not described in the literature.

0.1616 g substance: 0.1228 g $BaSO_4$ (Carius). Found % S 10.44. $C_{15}H_{16}O_3N_2S$. Calculated %. S 10.07.

It does not give the quinonebromimide reaction. It is more difficultly soluble in organic solvents than the corresponding amine. Hydrolysis of the acetyl derivative with caustic alkali gives the corresponding amine. After crystallization from alcohol the amine has m.p. 127.5°. It gives the quinonebromimide reaction. It is not described in the literature.

N³-Bromo-N⁴ p-toluenesulfonyl-2,5-toluquinonediimine



Prepared by the action of bromine on 5-amino-2-p-toluenesulfamidotoluene. After crystallization from dichloroethane (precipitation with alcohol) it forms a light yellow precipitate. M. p. 47°. Decomposes violently at 170°. It is readily soluble in dichloroethane and benzene, less readily soluble in alcohol, insoluble in water. With phenol in an ammoniacal medium and with 1-naphthol it forms a deep blue color. It liberates iodine from acidified iodide solutions.

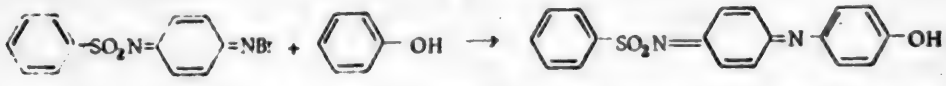
Analysis was effected by determination of the oxidation equivalent and by Carius determination of sulfur.

0.0454 g substance: 5.2 ml 0.1 N $Na_2S_2O_3$ 0.1236 g substance: 14.12 ml 0.1 N $Na_2S_2O_3$. Found: equiv. 87.58, 87.56. $\frac{1}{4}$ $C_{14}H_{13}O_2N_2BrS$. Calculated: equiv. 88.06. 0.1600 g substance: 0.1042 g $BaSO_4$ (Carius). Found %: S 8.95. $C_{14}H_{13}O_2N_2BrS$. Calculated %: S 9.11.

Study of the indophenol reaction of N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine

There are indications in the literature that joint oxidation with hypochlorite of N-p-toluenesulfonyl-1,4-phenylenediamine and phenols leads to formation of arylsulfonated indophenols [9]. We have attempted to prepare a similar compound by reaction of N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine with phenol.

The proposed reaction should proceed according to the scheme:



The reaction was conducted in an aqueous-alcoholic ammonia solution and the reaction mixture was treated with benzene; the benzene layer was removed and contained the unreacted phenol and quinonediimine; the indophenol was extracted from the aqueous layer with butyl alcohol. Evaporation of the butyl alcohol at low temperature left a resinous material fromwhich the indophenol was extracted with dilute ammonia solution. The filtered solution was acidified with acetic acid. The resultant dark flocs acquired a deep violet color after drying and melted unsharply with preliminary sintering at 188°. All attempts to crystallize the material from a solvent were unsuccessful, so that analysis was performed on the crude product.

0.1587 g substance: 0.1086 g $BaSO_4$ (Carius). Found %: S 9.40. $C_{18}H_{14}O_3N_2S$. Calculated %: S 9.47.

Consequently it would appear that the bromine in N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine reacts with phenols to form an arylsulfonated indophenol.

SUMMARY

1. Four N-bromo-N'-arysulfonylquinonediimines and one N-chloro-N'-arylsulfonylquinonediimine have been prepared for the first time and their properties have been described.

2. The prepared compounds quantitatively liberate iodine from acid solutions of iodides, and the oxidation equivalent is found to be one-quarter of the molecular weight.

3. The reaction of N-bromo-N'-benzenesulfonyl-1,4-benzoquinonediimine with phenol in an ammoniacal medium is described; it forms an indophenol containing sulfur.

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[8] Morgan, Micklewait, J. Chem. Soc., 87, 1303 (1905).

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• See Consultants Bureau translation, p. 1917.
•• See Consultants Bureau translation, p. 1059.
••• See Consultants Bureau translation, p. 1053.
•••• See Consultants Bureau translation, p. 1901.

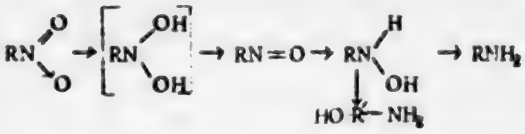
ELECTROLYTIC REDUCTION OF HALOALKYL-SUBSTITUTED AROMATIC NITRO COMPOUNDS

V. M. Berezovsky and V. S. Varkov

The utilization of noble metals as catalysts in the reduction of haloalkyl-substituted aromatic nitro compounds permits the reaction to be carried out in a medium of inorganic or organic acid or in a neutral medium, i.e., in conditions favoring the formation of primary amines and replacement of an atom of chlorine by hydrogen. Catalysts of nonnoble metals must be used in an alkaline or neutral medium. One of us has shown [1] that the process of alkaline reduction of 2-chloro-methyl-4-nitrotoluene in specially selected, narrowly maintained, reaction conditions can be directed in such a manner that the main reaction product is a primary amine; during the reaction the chlorine atom is eliminated. By this method the hydrogenation of 2-chloromethyl-4-nitrotoluene in alcoholic alkaline medium with a skeletal Ni catalyst gives o-4-xylidine in 50-70% yield. This reaction is accompanied, however, by other reactions which are characteristic of alkaline reduction and which become the predominant reactions if the conditions deviate from those selected; in such cases azoxy compounds and other products of alkaline reduction are formed. More consistent reductions to the primary amine were only obtained by using high dilutions (60- to 80-fold) of the starting substance.

With the objective of establishing more favorable conditions for formation of the primary amine and for elimination of the chlorine atom from the aliphatic substituent, we employed electrolytic processes which are widely used for effecting a variety of chemical transformations of organic compounds, e.g., the stepwise reduction of nitro compounds, various oxidation reactions, introduction of halogens into molecules, and even for nitrations [2], etc.

During the cathodic process the aromatic nitro compound is initially reduced to the dihydroxamine [3] which is then dehydrogenated to the nitrosocompound; this reaction takes place at high velocity. In the next stage of the process the nitroso compound is readily reduced to arylhydroxylamine. In an alkaline or neutral medium the latter compound undergoes further reduction very slowly and chemical condensation processes predominate in the first stage. Reduction of arylhydroxylamines in an acid medium proceeds at an adequately high velocity (although still more slowly than its rate of formation from the nitroso compound), thereby avoiding chemical condensation processes, and leads to formation of primary amine in high yield when a suitable metal is selected for the cathode. The acidic reduction of aromatic nitro compounds may be represented by the following scheme:

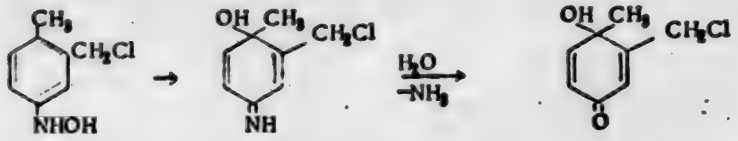


The halogen of the nucleus is not substituted by hydrogen by the electrochemical route [4], and only one nitro group is reduced in chloronitro compounds. e.g., from p-chloronitrobenzene we obtain p-chloroaniline and from chlorodinitrobenzene we obtain chloronitroaniline. These facts demonstrate the negative influence of the halogen of the aromatic nucleus on the reduction of the nitro group of this ring. In certain conditions of electrolytic reduction the reduction of the nitro group is accompanied by replacement of a chlorine atom, not by hydrogen but by hydroxyl; for instance, from p-chloronitrobenzene we get p-aminophenol. Reduction of aliphatic nitro compounds proceeds with difficulty by the electrolytic route with formation of a mixture of products with a lower degree of chlorination, while methyl chloride practically does not split off halogen [4]. Carbon tetrachloride is not reduced at a platinum cathode, while at a copper and lead cathode reduction takes place only with formation of chloroform. It is therefore clear that it is much more difficult to reduce the chlorine atom than it is to reduce the nitro group, all the more since the results of electrolysis depend in high degree on the magnitude of the overvoltage, the concentration of the substance which is being reduced and other experimental conditions.

In this investigation we have studied the effect of various factors (composition of the medium, the material of the cathode, the temperature, the current density, etc.) on the formation and yield of o-4-xylidine by electro-

lytic reduction of 2-chloromethyl-4-nitrotoluene. In this process it is possible to employ as the catholyte solutions of the substance in aqueous ethyl alcohol [5] and acetic acid [6]. We have shown, however, that there are considerably greater advantages in utilizing 2-chloromethyl-4-nitrotoluene in the form of a suspension.

A small amount of ammonia is found to be evolved when the xylidine is distilled off from the neutralized electrolytic solutions. This may be accounted for on the basis of the following mechanism of the side reaction proceeding during acidic reduction. During the second part of the cathodic process, when the arylhydroxylamine has already been formed, the latter is rearranged under the influence of sulfuric acid to form a quinolimine containing a quinoid nitro group; this imino group is hydrolyzed by acid with formation of ammonia, and at the same time is replaced by oxygen:

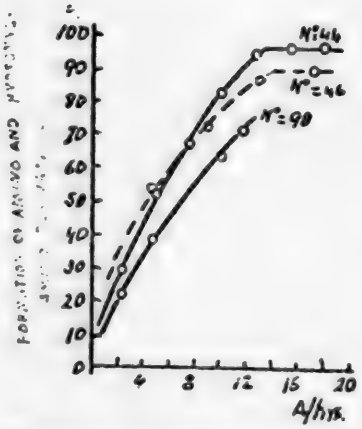


The final product of this rearrangement and hydrolysis is quinol. The proposed reaction mechanism is consistent with known data for p-tolylhydroxylamine [7]. The observed decrease in yield of primary amine with rising current density, which is associated with electric and thermal phenomena, may also be governed by the intensification of this side reaction.

The velocity of reduction of the nitro group, as shown in numerous examples, is higher than the velocity of chlorine removal; hence the velocity of formation of the arylhydroxylamine must be higher than that of substitution of the chlorine atom by hydrogen. Consequently, during the first phase of the cathodic process 2-chloromethyl-4-tolylhydroxylamine must be formed; if its further reduction is retarded, then it undergoes rearrangement to the corresponding chloro-substituted quinolimine.

In the experimental conditions the formation of the primary amine does not proceed strictly in the sequence represented by the above formulas. In order to clarify the course of the process we performed analyses of the electrolyte for its content of primary and secondary amino groups and obtained the results plotted in the diagram.

Up to the maxima the plots in the diagram correspond to both NHOH- and NH_2 groups. The inflection point corresponds to the completion of formation of hydroxylamine, and the remainder of the plot corresponds to the transformation of --NHOH-- into $-NH_2$ and is naturally a straight line. The inflection point lies between 11.5 and 13.5 A/hours; after this period analysis reveals the formation of 0.0460-0.0506 g-equiv. of compound containing NHOH- and NH_2- groups against the calculated amount of 0.0539 g-equiv., i.e., 85-93%. In these conditions, however, the yield in the form of xylidine is only 30.1% of the theoretical. Consequently the reaction of formation of the hydroxylamine is accompanied by its further reduction. At the same time a portion of the hydroxylamine undergoes the above-mentioned rearrangement. The absence of a second inflection point in the experimental conditions shows that the first stage of the reaction – formation of the nitroso compound – also proceeds side by side with the reduction of the NO group to NHOH and not strictly subsequent to it. Hence the process of electrolytic reduction of the nitro group of 2-chloromethyl-4-nitrotoluene at a lead cathode simultaneously involves the three stages of the reaction of acidic reduction.



Dependence of the formation of amino and hydroxylamino derivatives on the applied current.

The character of electrolytic reduction of organic compounds is profoundly influenced by the overvoltage. Reduction of aromatic nitro compounds at a platinum or nickel cathode readily proceeds to the hydroxylamine stage. The second stage of acid reduction – to the amine – proceeds with difficulty at these cathodes. Reduction of 2-chloromethyl-4-nitrotoluene to xylidine also proceeds unsatisfactorily at cathodes, such as Ni, with a low overvoltage, whereas good results are obtained at cathodes with a high overvoltage (Zn, Pb). However, unlike aromatic nitro compounds not containing haloalkyl substituents, 2-chloromethyl-4-nitrotoluene reduces unsatisfactorily to xylidine at certain cathodes with a high (Hg) and a medium (Cu) overvoltage, while the results are still less satisfactory at certain cathodes with a high overvoltage (Sn). We know that tin deposited in a finely divided state on the surface of a cathode of another

metal increases the yield of primary aromatic amines. This effect, as we have shown, is not manifested in the case of halogen-substituted aromatic nitro compounds when tin is deposited on a lead cathode. Replacement of ethyl alcohol by methyl alcohol leads to a serious drop in yield also at cathodes with a high overvoltage (Zn and, in particular, Pb), which illustrates the great influence of the medium on the electrolytic process.

Hence the character of the electrolytic reduction of halogen-substituted aromatic nitro compounds depends not only on the overvoltage which is associated with supplementary polarization of the cathode, but also on the catalytic action of the metal cathode. The most active catalyst is zinc; leads exhibit a less intense catalytic action; tin is completely devoid of catalytic activity.

EXPERIMENTAL

Electrolytic reduction of 2-chloromethyl-4-nitrotoluene. The apparatus consisted of a 2-liter glass beaker containing a porous glass diaphragm 84 mm in diameter and 180 mm high with a glass thickness of 4 mm. In the anodic space between the porous and the glass beakers a cylindrical lead anode was located. The anolyte was 10% sulfuric acid. In the cathode space inside the porous beaker was located a cathode made of various metals in the form of a perforated cylinder or spiral tube, a glass coil for cooling, a glass mechanical stirrer and a thermometer. The catholyte was a suspension of 2-chloromethyl-4-nitrotoluene in an aqueous or aqueous-alcoholic medium (1:30), containing 6.3 g sulfuric acid in 100 ml (1.3 N) or a suspension in aqueous acetic acid. The starting material for the investigation was 2-chloromethyl-4-nitrotoluene with the following characteristics:

M.p. 52-55°; Cl (hydrolyzable) 19.42%, Cl (inorganic) 0.82%; NO_2 21.66%; water 1.0%. $C_8H_8O_2NCl$. Calculated %: Cl (hydrolyzable) 19.11; content of 2-chloromethyl-4-nitrotoluene,%: from Cl content 101.4; from NO_2 content 87.1.

The amount of 2,6-bis-chloromethyl-4-nitrotoluene in crude 2-chloromethyl-4- nitrotoluene was determined by the following method: 50 g pulverized 2-chloromethyl-4-nitrotoluene was dissolved in 200 ml methyl alcohol at 35-40°, the solution was filtered from turbidity and left till the next day at room temperature. 6.1 g crystals came down with m.p. 139-144°; these were fairly pure 2,6-bis-chloromethyl-4-nitrotoluene. % content of 2,6-bis-chloromethyl-4-nitrotoluene: from Cl content 94.4; from NO_2 content 98.1.

It therefore follows that the starting material contains 87.8% 2-chloromethyl-4-nitrotoluene. All the yields calculated below were based on this assumption.

Electrolytic reduction proceeds according to the equation:

$$ClCH_2C_7H_6NO_2 + 8H^+ + 8e \rightarrow C_8H_9NH_2 + 2H_2O + HCl,$$

and consequently the reduction of 1 mole 2-chloromethyl-4-nitrotoluene will consume 25.86 X 8 ≈ 215 A/hours.

With progressive electrolytic reduction in the alcoholic electrolyte, the suspension of 2-chloromethyl-4-nitrotoluene gradually went into solution. At the conclusion of the electrolysis the nearly transparent solution was filtered (the residue was mainly the more difficultly soluble 2,6-bis,chloromethyl-4-nitrotoluene); the solvent was distilled off, toward the end with steam. The aqueous residue was treated with 10% sodium hydroxide until a permanent red color was imparted to phenol phthalein paper, after which the separated o-4-xylidine was distilled off with steam. Ammonia was detected during the initial distillation. The aqueous distillate was cooled, and after separation of the crystalline product the liquor was again steam-distilled. o-4-Xylidine was obtained in the form of faint yellow crystals analyzing (nitrite method) at 95.5, 96.7, 94.1, 95.5, 98.1% or an average of 96%. After purification by vacuum distillation, the product melted at 48-49°.

Found %: N 11.68 (Kjeldahl). $C_8H_{11}N$. Calculated %: N 11.57.

Influence of the medium (solvent) on the electrolytic reduction. The effect of various solvents on the xylidine yield was studied in a series of reductions of 2-chloromethyl-4-nitrotoluene at a Pb cathode with a current density of D 2.5A/dm^2, a temperature of 28-30°, a current consumption of 25 A-hours (110% excess over the theoretical), electrolysis was effected at a voltage of 5-6 V. 10 g of 2-chloromethyl-4-nitrotoluene was used in each experiment. The suspension of 2-chloromethyl-4-nitrotoluene did not go into solution completely when using a catholyte of methyl alcohol, acetic acid or water. The experimental results are presented in Table 1.

The fall in yield of xylidine in dilute alcohol solutions and even more so in water is the natural consequence of the decreasing solubility of 2-chloromethyl-4-nitrotoluene. Electrolytic reduction also takes place in acetic acid but the xylidine yield is quite unsatisfactory. The drop in yield when using methyl alcohol is noteworthy.

TABLE 1

Expt. No.	Solvent	Yield of xylidine (%)
60	75% ethyl alcohol	72.0
63	30% ethyl alcohol	21.8
39	75% methyl alcohol	46.9
73	75% acetic acid	26.8
62	Water	5.0

TABLE 2

Expt. No.	Temp.	Yield of xylidine (%)
4	10°	8.4
56	21	68.6
60	30	72.0
85	30	72.0
47	38	72.0
7	42	67.0
7'	45	58.6

TABLE 3

Expt. No.	D, A/dm²	Yield of xylidine (%)	Expt. No.	D, A/dm²	Yield of xylidine (%)
21	1.0	62.3	54	2.5	69.6
28	2.0	67.0	46	4.5	72.0
32	2.5	70.4	69	6.0	64.0
60	2.5	72.0	25	8.0	57.0
85	2.5	72.0	75	10.0	45.2

Effect of temperature. The temperature effect was studied at between 10 and 45°. Experiments were performed in an electrolyzer with a Pb cathode in 75% ethyl alcohol in presence of sulfuric acid; D = 2.5 A/dm²; A-hours 25-30; weight of starting substance 10 g.

The results (Table 2) show that within the temperature range of 30 to 40° a change of temperature does not affect the yield. Higher temperatures reduce the yields and lower temperatures do so even more markedly.

TABLE 4

A-hours	11.5	15	25
No. of expt.	98	48	60
Yield of xylidine (%)	31.7	45.3	72.0
Current yield (Y%)	29.3	32.0	30.0

Current density. The effect of change of current density on the reduction of 2-chloromethyl-4-nitrotoluene was studied over the range of 1 to 8 A/dm². The same apparatus as before was used in the same conditions except for the variation of current density (Table 3).

We see from Table 3 that the yield is not affected by a change in current density between 2 and 4.5 A/dm². A marked drop in yield follows the raising of the current density to 8 A/dm² or its fall to 1 A/dm².

TABLE 5

Expt. No.	A/dm²	Xylidine yield (% of theory) in dependence on the cathode material (in ethyl alcohol)						
		Zn	Pb	Sn on Pb	Hg	Cu	Ni	Sn
24	2.5	78.7	–	–	–	–	–	–
60	2.5	–	72.0	–	–	–	–	–
85	2.5	–	72.0	–	–	–	–	–
92	2.5	–	70.4	–	–	–	–	–
32	2.5	–	70.4	–	–	–	–	–
57	2.5	–	–	62.8	–	–	–	–
58	2.5	–	–	58.9	–	–	–	–
15	2.5	–	–	–	52.0	–	–	–
16	2.5	–	–	–	52.5	–	–	–
88	2.5	–	–	–	–	45.2	–	–
87	6.0	–	–	–	–	–	20.1	–
8	2.5	–	–	–	–	–	–	10.0

Current yield. In our investigation of the effect of various factors on the electrolytic reduction of 2-chloromethyl-4-nitrotoluene we calculated the yield on the basis of the amount of substance formed with an amount of current sufficient for definite completion of the process. It is also of interest to determine the current yield of xylidine (Y%), as defined by the formula:

$$Y\% = \frac{M \cdot 100}{0.562\ Q},$$

where M is the weight of xylidine formed; 0.562 is the theoretical amount of xylidine formed under the action of 1 A/hour; Q is the amount of consumed electricity (in A-hours).

Experiments were performed in 75% ethyl alcohol with the usual ratios of reagents at 30° (Table 4).

Complete reduction of 2-chloromethyl-4-nitrotoluene theoretically requires 11.5 A-hours.

Dependence of the electrolytic reduction on the cathode material. Cathodes of Hg, Pb, Zn, Sn, Cu and Ni were employed. Experiments were performed in 75% ethyl alcohol in presence of sulfuric acid at 28-30°; weight of starting material 10 g. Results are presented in Table 5.

TABLE 6

Expt. No.	A/dm²	Xylidine yield (% of theory) in dependence on the cathode material (in methyl alcohol)					
		Zn	Pb	Hg	Cu	Ni	Sn
66	2.5	68.6	–	–	–	–	–
39	2.5	–	46.9	–	–	–	–
67	2.5	–	–	46.8	–	–	–
17	2.5	–	–	–	45.3	–	–
68	2.5	–	–	–	–	16.7	–
65	2.5	–	–	–	–	–	11.7

TABLE 8

Expt. No.	Current passed, A-hours from start of expt.	NHOH and NH_2 content of solution calculated on the xylidine (in %)	Total content of NHOH and NH_2 groups calculated on xylidine (in g)
44	2.5	0.58	1.88
	5.0	1.02	3.44
	7.5	1.32	4.05
	10.0	1.60	4.96
	12.5	1.83	5.58
	15.0	1.86	5.58
	17.5	1.86	5.48
	20.0	1.86	5.39
46	5.0	1.08	3.34
	9.0	1.47	4.48
	13.0	1.77	5.31
	17.5	1.83	5.39
	21.5	1.80	5.22
98	2.5	0.45	1.44
	5.0	0.75	2.36
	10.0	1.25	3.78
	11.5	1.40	4.20

TABLE 7

Expt. No.	% Content of suspension	D A/dm²	Xylidine yield (%)
54	3.3	2.5	69.6
85	3.3	2.5	72.0
26	6.6	4.0	74.0

The series of metals – Sn, Ni, Cu, Hg, Pb, Zn – arranged in order of increasing yield of xylidine has a different order from that of the metals in the overvoltage series. Slightly different results are obtained when the electrolysis is carried out in methyl alcohol. The order of the metals, when arranged in accordance with increasing yields of xylidine, remains the same, but the yield is strongly reduced at the zinc and, in particular, at the lead cathode (Table 6).

Effect of concentration of substance on yield. Several experiments were performed at a lead cathode in 75% ethyl alcohol in presence of sulfuric acid (Table 7).

When the catholyte contains 3.3-6.6% starting material, the yield of xylidine is seen to be almost constant.

Formation of primary and secondary amino groups during the reaction. The proportions of primary and secondary amino groups formed during electrolysis were determined by the following procedure: 5 ml electrolyte was filtered from the precipitate and titrated in a strongly acid medium (while cooling) with 0.05 N sodium nitrite solution. The analytical results of three experiments are detailed in Table 8 and plotted in the diagram. 10 g starting material was used in each experiment.

In conclusion we express our gratitude to V. A. Devyatina and L. N. Kravchina for performing the analyses.

SUMMARY

1. A study was made of the dependence of the electrolytic reduction of halo-alkyl-substituted aromatic nitro compounds on the cathode material, the medium, the temperature, the current density and other factors.

2. It was shown that the electrolytic reduction of 2-chloromethyl-4-nitrotoluene proceeds with increasing yields of the xylidine in the following order of cathode materials: Sn, Ni, Cu, Hg, Pb, Zn.

3. The difference between this order and the order of the metals in the overvoltage series is explained by the catalytic action of the cathode material.

4. The most active catalyst for the electrolytic reduction of haloalkyl-substituted aromatic nitro compounds is zinc; next in order is lead; complete absence of catalytic action is found with tin.

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THE MECHANISM OF THE REACTION OF CHLOROSULFONIC ACID WITH SOME AROMATIC COMPOUNDS

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The problem of the mechanism of reaction of chlorosulfonic acid with aromatic compounds had not been closely studied up to now and has remained controversial. Thus in a monograph on the sulfonation of organic compounds, I. S. Ioffe [1] bluntly states that "...up to now the course of the reaction of chlorosulfonic acid with sulfonatable substances is unclarified". The theory is extremely widespread that the first products of the reaction are sulfochlorides:

$$ArH + ClSO_3H \longrightarrow ArSO_2Cl + H_2O. \qquad (1)$$

The released water decomposes the excess of chlorosulfonic acid into hydrogen chloride and sulfuric acid; the latter sulfonates the organic compound to give sulfonic acids as by-products. Consequently the presence of sulfonic acids is regarded as the result of a secondary sulfonation reaction with sulfuric acid [2,3,4,5]. This theory does not appear to have been experimentally confirmed at any time; as will be shown below, it does not reflect the actual course of the reaction with sufficient completeness and accuracy.

Experimental studies with various compounds—toluene [6], naphthalene [7] and acetanilide—have shown that for these compounds the reaction is more correctly represented on the basis of initial formation of sulfonic acids by the action of chlorosulfonic acid:

$$Ar\,\boxed{H} + \boxed{Cl}\,SO_3H \longrightarrow ArSO_3H + HCl. \qquad (2)$$

Subsequently the sulfonic acids are transformed into sulfochlorides according to the scheme:

$$ArSO_2\,\boxed{OH} + HSO_3\,\boxed{Cl} \longrightarrow ArSO_2Cl + H_2SO_4. \qquad (3)$$

According to this mechanism sulfonic acids are mainly formed as the result of incompleteness of the chlorosulfonation reaction.

Clarification of the true mechanism of the reactions is very necessary for a realistic and efficient operation of the industrial processes for sulfochlorides, since the first theory indicates that the process should be interrupted at the earliest possible moment to give a maximum yield of sulfonic acids, while the second theory requires that the process should be prolonged until the maximum amount of sulfonic acids has been converted into sulfochlorides. The clarification of the mechanism of this complex reaction, which includes a series of parallel and consecutive processes, is greatly complicated by the formation sometimes in high yields, side by side with sulfonic acids and sulfochlorides, of sulfones, polysulfonated derivatives, chloro derivatives, side chain-substituted oxidation products and many other substances which undergo reciprocal transformations.

For the purpose of arriving at a preliminary solution of the main problem—the mechanism of the entry of the chlorosulfonic group into an organic molecule—we carried out some thermodynamic calculations. The changes of free energy and of entropy of the individual reactions were calculated for a series of aromatic compounds.

For the purpose of gaining insight into the mechanism of a reaction it is important to know not only the direction of the reaction and the degree of conversion—which are governed by the sign and magnitude of the free energy—but also the velocity of the individual reaction steps. The reaction velocity is governed, according to modern concepts, by the probability of formation of an active complex; in this connection the probability factor P appears to be related to the entropy of activation ΔS^* by the expression:

$$PZ = e^{\frac{\Delta S^*}{R}} \cdot \frac{kT}{h},$$

insofar as the theoretical number of collisions (Z), Boltzmann's constant (k), the gas constant (R) and Planck's constant (h) are substantially constant at the given temperature (T).

The lack of knowledge at the present time of the properties of the active complex is a serious hindrance to the calculation of the entropy of its formation. But since the active state exists between the commencing and final states, we can draw certain qualitative conclusions from a consideration of the total change of the entropy process ΔS.

We know that by using ΔS in place of ΔS^* for the evaluation of reaction velocity it is possible to arrive at serious deviations in the quantitative expression of the probability factor P, which plays an important part in the kinetic equation:

$$K_V = PZe^{\frac{-E}{RT}},$$

where K_V is the velocity constant and E is the activation energy.

However, for homogeneous reactions with structurally similar compounds existing in very similar states, a qualitative, roughly orientating, comparative evaluation of the reaction velocity with the help of ΔS can be performed with a measure of accuracy. Thus, if in the case of one of two heterogeneous reactions ΔS has a high positive value, then we must expect that the given reaction will be faster, while if the value is more negative then the reaction should be slower [17].

In other cases an evaluation of reaction velocity on the basis of ΔS will be less accurate. Nevertheless a comparison of the change of entropy of two similar reactions, especially when they differ not only in magnitude but also in sign, permits an evaluation of the degree of probability of the arbitrary occurrence of each of them in an isolated system, the probability being related in a definite manner to the velocity of the process.

We defined the entropy of a process at 25°C as the difference between the entropies of formation of the reaction products and the starting substances. The entropy of formation of all the compounds was calculated as the difference between the standard entropy of the compound and the standard entropy of the elements entering into it.

The entropy of the elements was taken from the data of Parks and Huffman [9] and the entropy of the compounds was calculated from the formulas of I. L. Strelkov [10].

TABLE 1

Calculated Values of Entropy Changes (ΔS in electrostatic units), Heats (ΔH in kcal) and Free Energy (ΔF in kcal) for Reactions of the Type:

A) $X{-}C_6H_5 + ClSO_3H \longrightarrow X{-}C_6H_4{-}SO_3H + HCl$;
B) $X{-}C_6H_5 + ClSO_3H \longrightarrow X{-}C_6H_4{-}SO_2Cl + H_2O$;
C) $X{-}C_6H_4{-}SO_3H + ClSO_3H \longrightarrow X{-}C_6H_4{-}SO_2Cl + H_2SO_4$.

X	Name of compound	A			B			C		
		ΔS	ΔH	ΔF	ΔS	ΔH	ΔF	ΔS	ΔH	ΔF
$-H$	Benzene	0	−31.4	−31.4	+ 1.0	−21.3	−21.0	+10.7	+ 4.1	+ 0.9
$-CH_3$	Toluene	− 2.6	−42.8	−42.0	−31.0	−36.9	−26.7	−19.0	+ 0.7	+ 6.6
$-NH_2$	Aniline	+ 1.2	−34.8	−35.2	−24.7	−26.8	−19.5	−13.8	+ 1.9	+ 6.0
$-NH\frac{CO}{2}$	Carbanilide	+24.5	−47.5	−54.8	+22.7	−41.4	−48.2	+17.2	−18.9	−24.0
$-NHCOCH_3$ . .	Acetanilide	+13.2	−32.3	−36.9	−13.1	−22.7	−19.1	−15.7	+ 3.9	+ 8.6
$-NHCOH$ . . .	Formanilide	+12.8	−61.8	−65.1	−13.2	−28.9	−24.3	−15.6	+26.7	+31.3

The solid substances at 298°K:

$$S_{298}^{\circ} = 2.0\,(C) + 2.5\,(H + N) + 4.4\,(O) + 10.0\,(Cl + Br + I) + 7.0\,(m).$$

For liquids at the same temperature:

$$S_{298}^{\circ} = 3.5\,(C) + 3.2\,(H) + 9.1\,(O) + 11.9\,(Cl + Br + I) + 9.8\,(N).$$

In these formulas C, H, N, O, Cl, Br, and I signify the number of atoms of the respective elements in a molecule, and m is the total number of other atoms.

The change of free energy of a process at 25°C was defined as the difference between the standard free energies of the products and the starting substances.

The free energy of the products ($\Delta F_{prod.}$) and the starting components ($\Delta F_{init.subs.}$) are calculated from the equation:

$$\Delta F_{298^\circ} = \Delta H - T\Delta S_{298^\circ}.$$

The heats of formation of the compounds from the elements $-\Delta H-$ were taken either from the literature or calculated from the equation:

$$\Delta H = H_{comb.} - [94.38\ (C) + 34.19\ (H) + 0(Br + Cl + I + N + O) + 41.4F + 69.3S].$$

In the case of absence from the literature of data for the heats of combustion ($H_{comb.}$) these were calculated from the Kharasch formula with corrections for the heat of fusion of solids.

Some of our calculated data are set out in Table 1.

It follows from consideration of these data that in the reaction of chlorosulfonic acid with aromatic compounds the formation of sulfonic acids and sulfochlorides is equally possible since the change of free energy of these processes has a large negative value. A comparison of the magnitudes of the change of entropy indicates, however, that the degree of probability of these processes is likely to vary with different compounds.

The probability of type A reactions for toluene, aniline, acetanilide and formanilide must be considerably higher than the probability of type B reactions, because in the first case the increase of ΔS is greater. This signifies that side by side with the direct formation of sulfochlorides proceeding at low velocity, the main mass must evidently be formed from sulfonic acids according to scheme (C) since the formation of the latter in scheme (A)must proceed with a higher velocity and with a higher yield.

In the case of carbanilide the entropy change of reactions (B) and (A) are substantially identical. It may be assumed that the formation of sulfonic acids as well as the direct formation of sulfochlorides must take place with similar velocities. Since, however, sulfonic acid formation involves a bigger drop in free energy, it will take place with a somewhat higher yield.

Formation of benzene sulfochloride according to schemes (A) and (B) also appears to have equal probability, although the first process must give a slightly higher yield. Benzene sulfochloride appears to be formed with similar velocities by both schemes. Formation of sulfochlorides according to scheme (C) at 25°C from toluene, acetanilide and formanilide will be hindered and will require a supply of heat from outside. In these conditions benzene sulfonic acid and the sulfonic acid of carbanilide must undergo ready transformation into sulfochlorides. These assumptions find confirmation in practical operation of the processes. Whereas the preparation of the sulfochlorides of toluene, acetanilide and formanilide can be effected either by reaction over a prolonged period or at a temperature of 60-80°, benzene sulfonic acid is obtained in good yield by reaction for a short period at 20-25°.

Thus the thermodynamic calculations show that in chlorosulfonation reactions formation must take place simultaneously of both sulfonic acids and (directly) of sulfochlorides. The degree of probability of these reactions depends on the type of starting compound and on the reaction conditions. It is consequently impossible to single out any one of the above schemes as corresponding to the mechanism of chlorosulfonation. In other words none of these schemes can be regarded as a general scheme of chlorosulfonation since it is always necessary to specify the type of compound used and the reaction conditions.

For the purpose of experimental verification of the conclusions reached from thermodynamic calculations, we performed a series of experiments on the influence of temperature, duration of reaction and ratios of components on the yields of sulfochlorides and sulfonic acids during chlorosulfonation of various aromatic compounds. Most of the experiments were performed by the following procedure:

With energetic stirring the organic compound was gradually added to the calculated amount of chlorosulfonic acid at a definite temperature which was maintained with the help of a thermostat. The resultant reaction mass was then held for a definite period at the specified temperature. The reaction was terminated and the product isolated by pouring the mass into a large volume of water at the given temperature under vigorous stirring. The products were liquids or solids and were separated from the aqueous solution, washed with distilled water until all traces of sulfuric and hydrochloric acids had been removed, dried to constant weight, and analyzed. The aqueous solution of organic substances and inorganic acids together with the wash waters was also analyzed. The organic compounds were sometimes isolated from this solution. For this purpose the solution was neutralized

with ammonia solution or 10% sodium hydroxide and evaporated to dryness, and the dry residue extracted in a Soxhlet with alcohol, acetone or other common solvent for removal of the organic compound.

TABLE 2

Yields of Sulfochlorides, Sulfonic Acids and Sulfones in the Chlorosulfonation of Aromatic Compounds over a Period of 2 Hours.

Expt. No.	Compound	Molar ratio of compound to chlorosulfonic acid	Temp. (°C)	Yields (mole-%)			
				of unreacted compound	of sulfochlorides	of sulfonic acids	of sulfones
1	Benzene	1:1	−40	46.5	Traces	53.2	Traces
2	"	1:1	25	—	7.8	89.2	3.0
3	"	1:1	90	—	12.0	80.2	7.7
4	"	2:1	25	—	4.9	—	4.3
5	Toluene	1:1	−40	63.5	Traces	35.2	—
6	"	1:1	25	—	4.6	87.2	4.5
7	"	1:1	90	—	10.3	•	9.7
8	o-Xylene	1:1	25	—	2.0	93.2	—
9	Naphthalene	1:1	25	—	3.2	94.6	—
10	Acetanilide	1:1	25	—	2.5	96.9	—
11	"	1:5	25	—	9.6	80.8	—
12	"	1:5	60	—	82.4	•	—
13	Carbanilide	1:1	25	—	9.2	•	—
14	"	1:5	25	—	28.2	•	—
15	"	1:5	60	—	65.3	•	—
16	Formanilide	1:1	25	—	2.5	98.0	—
17	"	1:5	25	—	11.0	88.3	—
18	"	1:5	60	—	75.2	•	—
19	Phenol	1:1	25	—	Traces	96.8	2.5
20	Nitrobenzene	1:1	25	—	1.8	94.2	2.7

The sulfochlorides were identified from their melting or solidifying points after purification (by vacuum distillation or recrystallization from benzene, acetone or dichloroethane). The sulfonic acids were identified by the melting points of their chlorides which were obtained by treatment of the sodium salts with phosphorus pentachloride; sometimes they were identified through the amides, prepared by the action of aqueous ammonia or ammonium carbonate on the sulfochlorides. For evaluation of the general course of the reaction (sulfonation, chlorination or chlorosulfonation), a sample of the reaction mass was analyzed for its content of organically bound sulfur and chlorine.

The experimental data (Table 2) show that sulfonic acids are the main products in the reaction of equimolar amounts of chlorosulfonic acid with aromatic compounds, the amount of sulfochlorides not usually exceeding 10% of theory. The amount of sulfonic acids considerably exceeds the amount of sulfochlorides in the first instant of reaction also when using large excesses of chlorosulfonic acid, particularly at low temperatur

The formation of a large amount of sulfonic acids in the first stage of the reaction may be explained both by the sulfonating action of chlorosulfonic acid and by the presence of sulfuric acid also formed by hydrolysis of chlorosulfonic acid by the water released in accordance with equation (1).

It can be shown with the help of thermodynamic calculations that sulfonation with chlorosulfonic acid must take place much more readily than sulfonation with sulfuric acid. In fact, applying Hess's law we see that the difference between changes of entropy, free energy and thermal effects for sulfonation of any organic compound according to the schemes:

• Yields of sulfonic acids not specified since mixtures of sulfonic acids with different degrees of sulfonation are formed.

$ArH + ClSO_3H \longrightarrow ArSO_3H + HCl$ and $ArH + H_2SO_4 \longrightarrow ArSO_3H + H_2O$,

can be numerically expressed by the change of these magnitudes for the process:

$$ClSO_3H + H_2O \longrightarrow H_2SO_4 + HCl.$$

For this process our calculations give a value for ΔS of approximately +10.46 electrostatic units, and for ΔF of about −20,430 cal.

Sulfonation with chlorosulfonic acid must consequently proceed more rapidly and with a higher yield of products than sulfonation with sulfuric acid.

These considerations are confirmed in practice. Thus, benzene [11], toluene [6,12] and acetanilide [13] are sulfonated by chlorosulfonic acid more rapidly and at a lower temperature; anthrone [14] does not form sulfonic acids under the action of sulfuric acid at 180° but is sulfonated by chlorosulfonic acid even at 60-70°.

In the light of the above facts it must be stated that, notwithstanding the opinions of many authors [2,3,4,5], the secondary reaction with sulfuric acid during the process of chlorosulfonation can scarcely play an essential part and recedes even further into the background at high concentrations of chlorosulfonic acid, particularly at the start of the process. The main mass of sulfonic acids formed by the process consists of products of reaction with chlorosulfonic acid [equation (2)] and not with sulfuric acid.

In the second stage of the process the sulfonic acids undergo conversion into sulfochlorides in accordance with equation (3). This reaction takes place slowly and in the majority of cases it requires energy from outside.

In Figure 1 is plotted the change in amount of organic sulfur (curves S) and organic chlorine (curves Cl) in course of time during the process of chlorosulfonation of acetanilide at 25 and 40°. We see from the curves that the amount of organic sulfur reaches a value of nearly 100% (calculated on the monosulfo derivative) almost immediately after completion of the make-up of the batch (i.e. within 15 minutes); it then remains nearly constant throughout the whole process. On the other hand the amount of organic chlorine and the corresponding amount of separated sulfochloride (curve CX) are respectively 10 and 20% after make-up and gradually rise to a maximum before slowly falling. Curve CK, representing the change in amount of sulfonic acid in the reaction mass, and curve CX form an almost symmetrical pair, which fact confirms the reciprocal transitions: sulfonic acid ⇌ sulfochloride. At temperatures above 40° in the case of acetanilide this symmetry is upset due to reactions of di- and trisulfonation.

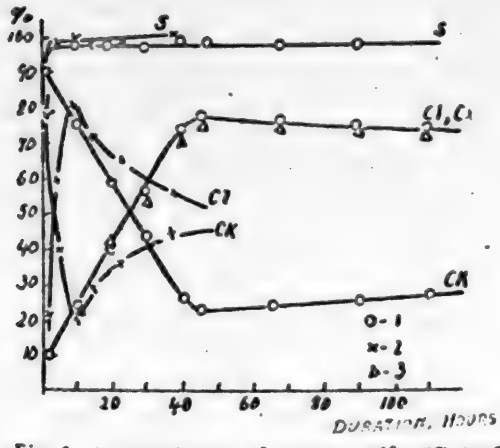


Fig. 1. Accumulation of organic sulfur (S) (in % of the theoretical for the monosulfochloride); organic chlorine (Cl) (in % of the theoretical for the monosulfochloride); yields of sulfochloride (CX) and of sulfonic acid (CK)(in % of the theoretical for chlorosulfonation of acetanilide). 1) at 25°; 2) at 40°; 3) sulfochloride at 25°.

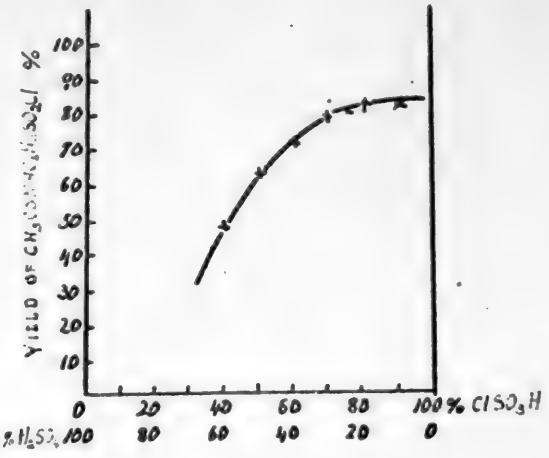


Fig. 2. Dependence of the yield of p-acetaminobenzene sulfochloride (in % of theory based on the composition of the inorganic portion of the reaction mass) at the conclusion of the process at 60°C in states close to equilibrium.

The course of curve Cl in Fig. 1 is characteristic of the chlorosulfonation of aromatic compounds in representing the kinetics of the slowest stage – the stage of transition of the sulfonic acid into the sulfochloride (equation 3).

It is reported in the literature [15] that at a temperature of about 100°, toluene sulfochloride is decomposed by sulfuric acid with formation of toluene sulfonic acid and evolution of hydrogen chloride and sulfur trioxide. We tested the possibility of effecting this reaction with various sulfochlorides at various temperatures. We established the general character of this reaction also at low temperatures (–40 and –20°C), when it may proceed with formation of chlorosulfonic acid:

$$ArSO_2Cl + H_2SO_4 \longrightarrow ArSO_3H + ClSO_3H.$$

Hence the reaction of formation of sulfochloride from sulfonic acid may be regarded as a reversible one. At normal and high temperatures it proceeds irreversibly due to dissociation of chlorosulfonic acid, which is caused by the influence of the large amount of heat released in the transition from sulfochloride to sulfonic acid:

$$ClSO_3H + 14.9_{cal.} \rightleftharpoons HCl + SO_3,$$

and the process can be essentially represented by the scheme:

$$ArSO_2Cl + H_2SO_4 \longrightarrow ArSO_3H + HCl + SO_3. \qquad (4)$$

An equilibrium is established between the concentrations of the products of reactions (3) and (4), which depends on the ratios of the velocities of these reactions at the given temperature. Due to this, in each such system it is only possible to obtain a certain yield of sulfochloride when the state of the system is close to equilibrium. Consequently the yield of sulfochloride depends, apart from the nature of the organic compound, the temperature and the duration of the process, on the composition of the reaction mass at the conclusion of the process, and, in particular, on the concentrations of chlorosulfonic and sulfuric acids; the latter, in turn, depend on the excess of chlorosulfonic acid used in the reaction and its concentration. This dependence is illustrated in Figure 2 for acetaminobenzene sulfochloride in states close to the equilibrium state.

Specially performed experiments showed that when the composition of the inorganic portion of the reaction mass at the conclusion of the process was 65% chlorosulfonic acid and 35% sulfuric acid, the molar ratio of benzene sulfonic acid to benzene sulfochloride at 25° was 0.3:0.7 irrespective of whether we started from benzene sulfonic acid and chlorosulfonic acid or from benzene sulfochloride and the calculated amount of a mixture of sulfuric and chlorosulfonic acids.

On the basis of the foregoing facts we can understand the course of the curve of change of amount of sulfochloride (CX) with passage of time (Fig. 1). In the rising branch of the curve, when the concentrations of sulfonic acid and chlorosulfonic acid are sufficiently high, reaction (3) predominates over reaction (4), in consequence of which the amount of organic chlorine increases and sulfochloride and sulfuric acid accumulate in the system. This progressively promotes the course of reaction (4), as a result of which the amount of sulfochloride begins to fall slowly after reaching a certain magnitude. The sulfochloride separated in accordance with reaction (4) again promotes reaction (3); hence with a large excess of chlorosulfonic acid the rate of fall of concentration of sulfochloride is very low. The course of curves (Cl) shows that the equilibrium state is not attained even after a long period, as it is hindered by the removal of hydrogen chloride from the sphere of reaction.

Apart from its theoretical interest, the curve in question has great practical significance. First it specifies the maximum yield of sulfochloride attainable at a given temperature and concentration of chlorosulfonic acid. Second, it indicates the necessity to interrupt the reaction at the maximum point, for further continuation of the process leads to a fall in the sulfochloride yield. This statement refutes the widely held opinion [16] that the reaction mass does not change after prolonged standing.

The above facts also compel us to reject the conclusion of L. S. Solodar [13] to the effect that sulfuric acid does not play a decisive part in the process of chlorosulfonation. Sulfuric acid plays an important part since, by lowering the concentration of chlorosulfonic acid and reacting with the resultant sulfochlorides, it must govern the yield of the latter.

It follows from curve (Cl) in Figure 1 that whereas the amount of chlorine increases relatively slowly, at the starting point immediately after addition of the organic compound (which takes a period of 15 minutes)

it has a value of about 10% of the theoretical. From this we must conclude that the presence of such a high percentage cannot be due to the transformation of sulfonic acid into sulfochloride [reaction (3)]. It is clear that for the greater part it could only have been formed at the expense of direct introduction of the SO_2Cl-group into the organic molecule by reaction with chlorosulfonic acid during the first stage of the reaction in accordance with equation (1); this is consistent with our preliminary conclusions reached on the basis of thermodynamic calculations.

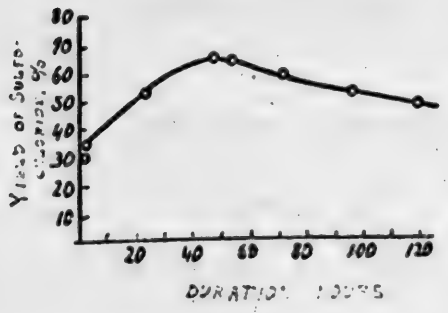
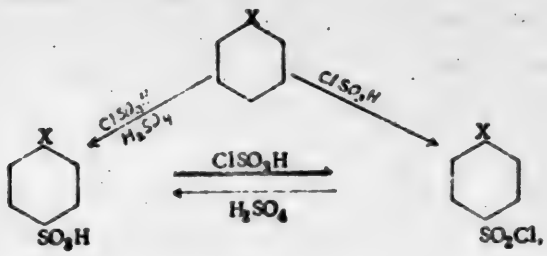


Fig. 3. Dependence of the yield of p,p'-disulfochloride of carbanilide on time during reaction at 25°.

According to these calculations (Table 1), reaction (1) for carbanilide at 25°C must proceed with a velocity much closer to that of reaction (2) than is the case for acetanilide. Experiment confirms this conclusion. Whereas the mean velocity of accumulation of chlorine in the reaction mass after the completion of the addition of material is 1.08% of the theoretical amount in an hour (Fig. 3), the amount of chlorine immediately after the addition (over a period of one half hour) was 30% of theory, reckoned on one SO_2Cl group per benzene ring.

On the basis of thermodynamic calculations and experimental data we may propose the following simplified scheme as being most probable for the reaction of chlorosulfonic acid with aromatic compounds:



where X is a substituent of the first order and the dense arrow indicates the preferred direction of reaction.

In this connection we must not forget that the true course of the reaction is considerably more complex and leads to the formation of a whole series of products: sulfones, polysulfo derivatives, chloro derivatives, products of side-chain substitution, etc. In the case, for example, of the reaction with aromatic acylamines, we have established that the first reaction products are acylsulfamino acids and their chlorides, which subsequently change into nuclear-substituted acylamines.

SUMMARY

1. On the basis of preliminary thermodynamic calculations and of experimental investigations a scheme has been established for the main reactions during chlorosulfonation of aromatic compounds with formation of chlorides of sulfonic acids.

2. It is shown that in the first rapid stage of the reaction between chlorosulfonic acid and the majority of aromatic compounds, the main products are sulfonic acids, while sulfochlorides are obtained in minor amounts. Sulfonation with sulfuric acid, when using high concentration of chlorosulfonic acid, does not play an important part.

3. In the second, slow, stage of the process the sulfonic acids are transformed into sulfochlorides under the action of excess of chlorosulfonic acid, and sulfuric acid is released. The reaction may be reversible at low temperatures and proceeds irreversibly at elevated temperatures due to breakdown of the chlorosulfonic acid (released during the reversible reaction) into sulfur trioxide and hydrogen chloride, and removal of the latter from the sphere of reaction.

4. Sulfuric acid plays an important part during chlorosulfonation, lowering the concentration of chlorosulfonic acid and reacting with the sulfochlorides to convert them into sulfonic acids. Consequently its presence in the reaction mass governs the yield of sulfochlorides in the given conditions for operation of the process.

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* See Consultants Bureau translation, p. 945.

THE PROBLEM OF THE THIOCYANATION OF o-NITROANILINE

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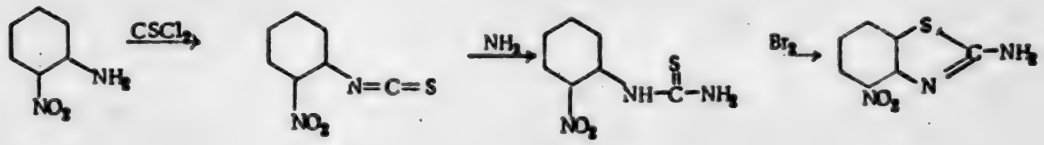
We required a supply of 2-amino-4-nitrobenzothiazole. In the literature we found three references to its synthesis.

1. The compound was prepared for the first time by Dyson, Hunter and Morris [1] from o-nitroaniline and thiophosgene according to the scheme:



They reported a m.p. of 232° for their 2-amino-4-nitrobenzothiazole.

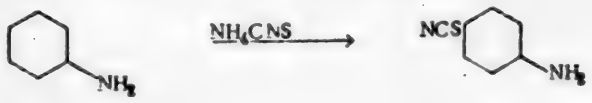
2. Erlenmeyer and Ueberwasser [2] improved the preceding method and obtained a nearly quantitative yield of 2-amino-4-nitrobenzothiazole with m.p. 254°.

3. Blomquist and Diuguid [3] obtained a compound with m.p. 110-112° by thiocyanation of o-nitroaniline by Kaufmann's method. They ascribed to this substance the structure of 2-amino-4-nitrobenzothiazole. After purification via the acetyl derivative the m.p. was raised to 130°. The acetyl derivative melted at 138-139°. Blomquist and Diuguid refer to the work of Dyson, Hunter and Morris; however the difference of 102° in the melting point of one and the same substance did not disturb them in the least. They then converted their amine into the chloro derivative by Sandmeyer's method and obtained a substance melting at 59.5-61.5°.

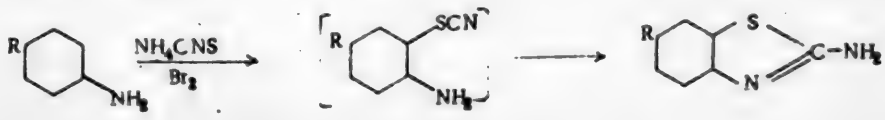
The authors assumed that they had obtained 2-chloro-4-nitrobenzothiazole, although Erlenmeyer and Ueberwasser 7 years previously had prepared 2-amino-4-nitrobenzothiazole and from it had obtained, via the diazo compound by Sandmeyer's method, 2-chloro-4-nitrobenzothiazole with m.p. 169-170°.

We were astonished not only by the discrepancy in the melting points but also because the American chemists, Blomquist and Diuguid, had applied Kaufmann'smethod without bothering to mention the fact.

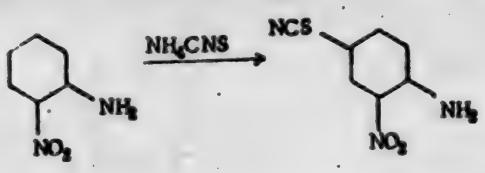
According to Kaufmann [4] and other workers [5], the first stage in the thiocyanation is the substitution of a thiocyanogen group for a hydrogen atom in the para-position to the amino group:



If the para-position is occupied, then substitution takes place in the ortho-position to the amino group and is accompanied by cyclization to a derivative of 2-aminobenzothiazole:



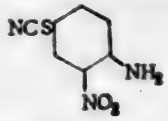
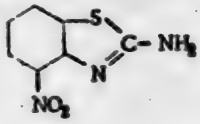
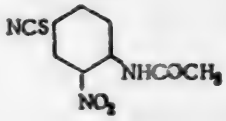
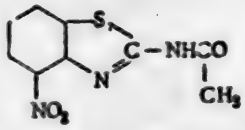
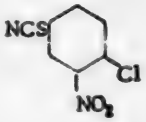
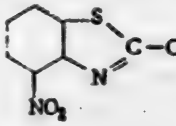
Consequently in the thiocyanation of o-nitroaniline by Blomquist and Diuguid in their specified conditions, only 2-nitro-4-thiocyanoaniline could be formed and not a derivative of 2-aminobenzothiazole.



The empirical formulas of 2-nitro-4-thiocyanoaniline and 2-amino-4-nitrobenzothiazole are identical. Hence the analytical data cannot be regarded as proof of the correctness of the authors' claims.

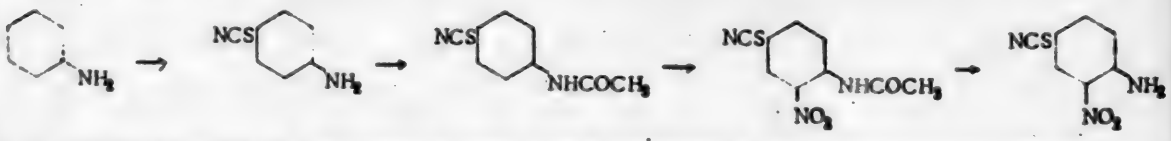
The following table presents data reported in the literature [6] for 2-nitro-4-thiocyanoaniline (I), 2-nitro-4-thiocyanoacetanilide (II) and 2-nitro-4-thiocyanochlorobenzene (III).

On the right, for comparison, are shown the melting points of the corresponding derivatives prepared by Blomquist and Diuguid by thiocyanation of o-nitroaniline and by replacing the amino group by chlorine:

Preparation No.	Thiocyano derivatives		Preparations of Blomquist and Diuguid	
	Structure	m.p.	Structure attributed by the authors	m.p.
I		113°		110-112°
II		138-139		138-139
III		63		59.5-61.5

We see from the table that the melting points of the corresponding compounds are the same or nearly so.

In order to prove that the product obtained by Blomquist and Diugid by thiocyanation of o-nitroaniline is not 2-amino-4-nitrobenzothiazole but 2-nitro-4-thiocyanoaniline, we prepared the latter by the following scheme as given in the literature [6]:



In the conditions described by the authors we obtained from o-nitroaniline the alleged 2-amino-4-nitrobenzothiazole and its acetyl derivative. The melting point of a mixed sample of 2-nitro-4-thiocyanoacetanilide with the acetyl derivative of the alleged 2-amino-4-nitrobenzothiazole did not suffer any depression. Nor was any depression observed in the determination of the mixed melting point of 2-nitro-4-thiocyanoaniline with the alleged 2-amino-4-nitrobenzothiazole.

There can thus be no doubt at all that Blomquist and Diuguid obtained 2-nitro-4-thiocyanoaniline in the thiocyanation of o-nitroaniline, and not 2-amino-4-nitrobenzothiazole. The compound which they prepared by replacing the amino group by chlorine was 2-nitro-4-thiocyanochlorobenzene and not 2-chloro-4-nitrobenzothiazole.

SUMMARY

It is shown that Blomquist and Diuguid obtained 2-nitro-4-thiocyanoaniline by thiocyanation of o-nitroaniline, and not 2-amino-4-nitrobenzothiazole as they erroneously concluded.

They obtained 2-nitro-4-thiocyanoacetanilide on acetylation of the product, and not 2-acetamino-4-nitrobenzothiazole; by diazotization followed by treatment with cuprous chloride these authors obtained 2-nitro-4-thiocyanochlorobenzene to which they erroneously ascribed the structure of 2-chloro-4-nitrobenzothiazole.

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CHLOROMETHYLATION OF ARYL ALIPHATIC KETONES

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The introduction of the CH_2Cl group into the aromatic nucleus with the help of CH_2O + HCl (the chloromethylation reaction) is one of the best established and most important reactions of organic synthesis in the aromatic series. Up to the present, however, there has been no known instance of the introduction of the CH_2Cl group into a chain even when special attempts have been made to effect such a reaction [1]. In July 1936 the successful chloromethylation of a series of aliphatic ketones was reported [2]:

$$R{-}CO{-}CH_3 + CH_2O + HCl \rightarrow R{-}CO{-}CH_2{-}CH_2Cl + H_2O.$$

Spurred on by this success, Fuson and McKeever [3] attempted to effect chloromethylation in the chain in a series of aliphatic-aromatic ketones. Success in this attempt would have provided a simple and accessible method of preparation of technically important vinylaryl ketones [4]. The authors did not achieve their objective: in the case of arylalkyl aliphatic-aromatic ketones chloromethylation did take place but the CH_2Cl group entered the ring and the aliphatic chain was not attacked; in the particular cases of acetophenone and propiophenone the reaction did not generally take place. It would thus appear that it is not possible to introduce the CH_2Cl group into a side chain by the chloromethylation reaction.

By using boron fluoride etherate $(C_2H_5)_2O{\cdot}BF_3$ as the catalyst* and monochlorodimethyl ether as the chloromethylating component, however, we have succeeded in effecting side-chain chloromethylation of acetophenone and propiophenone.

EXPERIMENTAL

1. Chloromethylation of propiophenone. Here we shall describe only one experiment; identical results were obtained in all the other experiments. In a thick-walled flask a mixture was prepared of 13.4 g (0.1 mole) propiophenone (B. p. 214-216°), 8 g monochlorodimethyl ether (b.p. 49-70°)** and 2.27 g boron fluoride etherate (b.p. 124-128°). The flask was tightly corked and heated in a water bath for 31 hours at 60-65° and for 1 hour at 80°. After cooling to room temperature, the reaction mass was poured into a separating funnel containing iced water, the water layer was separated, and the remainder was also washed with iced water until the reaction for boron was negative. The product was then dried over freshly calcined sodium sulfate and vacuum distilled.

12.93 g of material was fractionated: Fraction 1, 99-115° (6.5 mm), 6.84 g; fraction 2, 124-134° (6.5 mm), 4.20 g; residue, 1.25 g; losses, 0.64 g.

The first fraction proved to be unreacted ketone. The second fraction was a colorless liquid with a pungent odor, fuming in the air; it darkened on standing. Its properties were thus reminiscent of known β-chloroketones of the aliphatic series [2]. On repeated distillation nearly the whole came over at 115-120° (1 mm); d_4^{20} 1.1130; n_D^{20} 1.5326. Yield 23.1% of theory, calculated on the total ketone used, and about 47% calculated on the reacted ketone.

0.1814 g substance: 0.1300 g AgCl. 0.1608 g substance: 0.1155 g AgCl. 0.1620 g substance: 18.41 g C_6H_6: Δt 0.262°. 0.1473 g substance: 14.75 g C_6H_6: Δt 0.290°. Found %: Cl 17.69, 17.72; M 176, 181. $C_{10}H_{11}OCl$. Calculated %: Cl 19.45; M 182.5.

The low halogen content found may be due to partial hydrolysis of the chloromethylated product during washing (as well as to partial cleavage of HCl during the distillation).

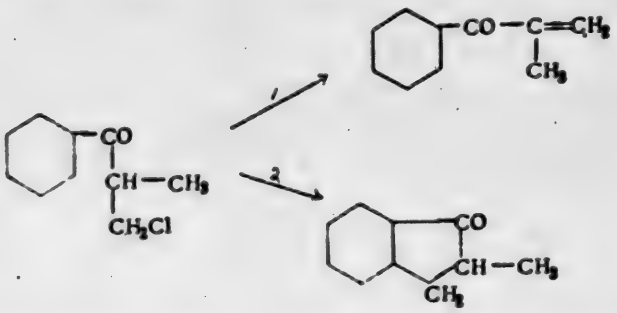
Oxidation: The position of the CH_2Cl group in the molecule of the prepared product was determined by oxidation. 2.4 g product was emulsified with 22 ml 17% sodium hydroxide solution and addition was made at room temperature in small portion of 262 ml 5% $KMnO_4$. The mixture was then heated on the water bath (60-70°) for 4 hours. The excess of permanganate was deoxidized by careful addition of formaldehyde solution. The filtered precipitate was twice digested with water (50 ml each time). The aqueous extracts were combined with.

*BF_3 has not previously been applied as a catalyst in the chloromethylation reaction.

**The reaction failed when using purer monochlorodimethyl ether (b.p. 54-60°) as the chloromethylating agent. The reason for this remains unexplained.

the filtrate, and the solution, after concentration on the water bath to a volume of 50 ml, was filtered through a small filter; the residue on the filter was washed 3 times with water (about 2-2.5 ml portions). Acidification of the filtrate with 10% H_2SO_4 caused a fine crystalline precipitate to separate. The precipitate dissolved when heated, and on slow cooling well-formed colorless platelets crystallized out. Yield of air-dry crystals 1.25 g or 78.1% of the theoretical; m.p. 118-122° and, after sublimation, 119-121.5°. A sample did not depress the melting point of benzoic acid. Titration with alkali confirmed that benzoic acid had been prepared. This also served as evidence that the CH_2Cl group is not introduced into the ring but into the side-chain, so that the obtained compound must have the structure: $C_6H_5COCH(CH_3)CH_2Cl$.

Cleavage of HCl. Two reactions are possible in the cleavage of HCl:



The possibility of the second direction is confirmed to some extent by the analogy with Fuson's experiment [5] when cleavage of water from methylolpropiophenone $C_6H_5COCH(CH_3)CH_2OH$ gave α-methylhydrindone instead of the expected phenylisopropenyl ketone.

5.45 g chloromethylated ketone and 5 g quinoline (m.p. 234-238°) were heated in a flask under a reflux condenser, protected with a $CaCl_2$ tube, at 70-80° (water bath) for 4 hours. The mixture was then distilled in vacuum when 6.32 g came over at 90-92° (1 mm), leaving a residue of 3.29 g (loss 0.46 g).

The distillate was washed with 5% HCl (to remove any quinoline which distilled over) and then with water until the reaction for halogen was negative. The washed distillate was dissolved in ether and dried with freshly calcined sodium sulfate. Removal of the ether left a colorless, transparent liquid with a negative reaction for halogen (Beilstein test). Yield 3.33 g or 76.2% of theory. Its pungent odor and irritant action on the eyes were strongly reminiscent of the commonest, simplest vinyl ketones (methyleneacetone, etc.).

d_4^{20} 1.0103; n_D^{20} 1.5342; MR_D 44.93. $C_6H_5COCH(CH_3)=CH_2$ MR_D 44.32; α-methylhydrindone MR_D 42.59

Oxidation (by the above-described method) gave benzoic acid in a yield of 52% of the theoretical. Phthalic acid would have been formed in the case of α-methylhydrindone, but was not found here. There was consequently no further doubt that, at any rate for the most part, the cleavage of HCl took place in direction 1 (see scheme above) and that the product was isopropenylphenyl ketone.

2. Chloromethylation of acetophenone. Following the experiment with propiophenone the chloromethylation of acetophenone (51.28 g, b.p. 201-204°) was performed by the same procedure except that the heating on the water bath at 60-65° lasted only 11 hours (due to the marked darkening of the mixture) instead of 31 hours (and 1 hour at 80°).

The washed and dried product (53.72 g) was vacuum-fractionated and gave: Fraction 1, 88-96° (12mm), 36.77 g; fraction 2, 96-107° (12 mm), 7.28 g. residue (viscous amber-colored resin), 8.94 g; loss 0.73 g.

A fresh distillation of the first fraction brought it over at 83-86° (11 mm); this was unreacted acetophenone. The second fraction was strongly reminiscent of the second fraction [b.p. 124-134° (6.5 mm)] of the preceding experiment: a colorless liquid with a pungent odor, fuming in the air, and darkening on standing. It gave a positive reaction in the Beilstein halogen test.

When redistilled it almost completely polymerized* (unexpectedly) to an undistillable, transparent, viscous mass with an amber color; only about 1 g distillate was obtained, while a small quantity of halogen-containing

* This fact alone is clear evidence that chloromethylation had taken place not at the ring but at the side-chain, since it is impossible to expect that compounds of the type of $ClCH_2C_6H_4COCH_3$ would polymerize so easily, or, indeed, that they would show any tendency at all to polymerize.

material crystallized at the end of the side tube of the distillation flask. After pressing on porous tile, the crystals melted at 46-49°. According to the literature [6] β-chloropropiophenone $C_6H_5COCH_2CH_2Cl$ melts at 57° and when distilled it partially changes into vinylphenyl ketone $C_6H_5COCH = CH_2$. It was clear in the light of all these facts that the product in the second fraction was mainly β-chloropropiophenone, i.e., in the case also of acetophenone the chloromethylation reaction took place and the CH_2Cl group entered the side chain.

Oxidation of the polymerized product gave benzoic acid in a yield of about 40% of the theoretical. Therefore these data likewise confirm out conclusion, for if chloromethylation had taken place at the ring, the structural unit of the polymer would have been a benzene ring with two side chains, and oxidation of such a polymer would have yielded phthalic acids.

SUMMARY

1. Side-chain chloromethylation was effected of acetophenone and propiophenone, although these compounds are reported in the literature to be not at all amenable to chloromethylation.

2. Cleavage of HCl from β-chloroisopropylphenyl ketone gave phenylisopropenyl ketone in 76% of the theoretical yield. The latter compound has not been described in the literature.

3. Boron fluoride etherate was used, for the first time, as catalyst in the chloromethylation.

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NEW OXIDATION REDUCTION INDICATORS

III. p- AND m-N-PHENYLAMINOBENZOIC ACIDS

V. M. Cherkasov

In one of the preceding publications [1] phenylanthranilic acid was proposed, for the first time, as an oxidation-reduction indicator. Within a short period phenylanthranilic acid found wide application in analytical chemical practice as an indicator with a high potential, and is now in general use. It was therefore natural that the possibility of using the isomers of phenylanthranilic acid, i.e., m- and p-phenylaminobenzoic acids, as oxidation-reduction indicators should be investigated. A comparative study of the three isomeric phenylaminobenzoic acids as oxidation-reduction indicators is also of theoretical interest, for such a study is bound to give some information on the dependence of the oxidation-reduction potential on the relative positions of the phenylamino and carboxyl groups in the benzene ring. Strange as it may seem, m- and p-N-phenylaminobenzoic acids have not hitherto been investigated, although attempts to prepare them have been reported in the literature [2].

The purpose of the present research was the preparation of m- and p-phenylaminobenzoic acids and of some of their derivatives and an exploratory study of these new compounds as oxidation-reduction indicators.

Goldberg [2] unsuccessfully attempted to prepare m- and p-phenylaminobenzoic acids by the action of m- and p-chlorobenzoic acids on aniline, or by the action of m- and p-aminobenzoic acids on bromobenzene in presence of copper powder. We, too, failed to obtain m- and p-phenylaminobenzoic acids when we repeated Goldberg's experiments.

It is known that the phenylation of aromatic amines proceeds most readily of all with aryl iodides [3,4], and least readily with aryl chlorides; we therefore decided to attempt the preparation of m- and p-phenylaminobenzoic acids by using the corresponding iodo compounds. By reacting iodobenzene with m- and p-aminobenzoic acids in presence of Cu powder, we prepared m- and p-phenylaminobenzoic acids, but only in low yields (~4%). Somewhat better yields 15, 17%) are obtained by the action of aniline on m- and p-iodobenzoic acids in presence of Cu powder.

p-Phenylaminobenzoic acid is a colorless crystalline compound with m.p. 158-159°; m-phenylaminobenzoic acid melts at 141-142°. Both acids are good oxidation-reduction indicators with a potential of about 1.12 V, i.e., very close to the oxidation-reduction potential of phenylanthranilic acid*. Consequently the position of the carboxyl in relation to the phenylamino group has no great influence on the magnitude of the oxidation-reduction potential. m- and p-Phenylaminobenzoic acids have no advantages over phenylanthranilic acid as oxidation-reduction indicators.

p-Phenylaminobenzoic acid was characterized by the preparation of its methyl ester and its hydrazide. Both of these substances gave a coloration with oxidizing agents in acid solutions, but they are unsuitable as indicators because the coloration is irreversible.

In conclusion we thank Professor A. V. Kirsanov sincerely for his advice during this investigation.

EXPERIMENTAL

p-N-Phenylaminobenzoic acid. A mixture of 9 g p-iodobenzoic acid, 9 g anhydrous potassium carbonate, 40 ml freshly distilled aniline and 0.2 g copper powder was refluxed under an air condenser for 15 hours. The

*Oxidation-reduction potentials were determined by V.S. Syrokomsky and V.V. Stepin in the laboratory of the Ural Institute of Heavy Metals.

aniline was distilled off in steam and the solution was filtered and acidified with hydrochloric acid. The precipitate was drained, washed with water and dried. p-Iodobenzoic acid was removed by treating the dry precipitate several times with hydrochloric acid sp. gr. 1.19.

The drained acidic filtrate was diluted with water, the precipitate was drained and washed with water. The dry substance was dissolved in cold benzene, the solution was treated with active carbon, the benzene was distilled off, and the crystalline residue, light yellow in color, was twice recrystallized from aqueous alcohol. Yield of pure product about 15% of the theoretical. p-N-Phenylaminobenzoic acid forms colorless needles, soluble in ether and benzene, less easily soluble in alcohol, and soluble with difficulty in water. M.p. 158-159° (uncorr.).

9.482 mg substance: 0.550 ml N_2 (11°, 746 mm). Found%: N 6.69. $C_{13}H_{11}O_2N$. Calculated %: N 6.56.

Methyl ester of p-N-phenylaminobenzoic acid. Methylation with dimethyl sulfate. 0.01 mole (2.13 g) p-N-phenylaminobenzoic acid was shaken for 15 minutes with 5.5 ml of 2 N sodium hydroxide and 1.40 g dimethyl sulfate, after which the mixture was heated on the water bath for 30 minutes. On cooling, 1.27 g crystalline product came down. Crystallization from ethyl alcohol gave the methyl ester of p-N-phenylaminobenzoic acid in the form of colorless needles with m.p. 115-116°; sparingly soluble in water, soluble in ether and benzene.

Methylation with diazomethane. To 1 g p-N-phenylaminobenzoic acid was added 60 ml of a solution of diazomethane in ether (from 5 ml nitrosomethylurethane). After the acid has dissolved, another 30 ml of solution of diazomethane in ether (from 2.5 ml nitrosomethylurethane was added. The ether was distilled off and the methyl ester of p-N-phenylaminobenzoic acid was recrystallized from alcohol to form colorless needles with m.p. 115-116°. It did not depress the melting point of the methyl ester prepared by reacting methyl sulfate with p-N-phenylaminobenzoic acid.

10.121 mg substance: 0.57 ml N_2 (12°, 747 mm). Found %: N 6.49. $C_{14}H_{13}O_2N$. Calculated %: N 6.26.

Hydrazide of p-N-phenylaminobenzoic acid. 0.45 g methyl ester of p-N-phenylaminobenzoic acid was heated on the water bath with excess of hydrazine hydrate for 5 hours. The cooled reaction mixture was diluted with water and acidified with dilute hydrochloric acid. The hydrazide of p-N-phenylaminobenzoic acid was precipitated from the solution with potassium hydroxide and after recrystallization from alcohol had m.p. 193-194°.

5.254 mg substance: 0.87 ml N_2 (13°, 740 mm). Found %: N 18.81. $C_{13}H_{13}ON_3$. Calculated %: N 18.50.

m-N-Phenylaminobenzoic acid. A mixture of 0.06 mole (14.7 g) m-iodobenzoic acid, 10 g potassium carbonate, 50 ml aniline and 0.2 g copper powder was refluxed under an air condenser for 15 hours. The aniline was distilled off in steam and the solution filtered and acidified with hydrochloric acid. The dry precipitate was extracted several times in the cold with benzene until the benzene-insoluble product failed to give a blue-violet color with bichromate in sulfuric acid. Distillation of the benzene left a yellow oil which crystallized after two days. The product was treated with sodium carbonate solution. The insoluble portion (the main mass) after washing with water did not give a coloration with bichromate. The product was precipitated from the sodium carbonate solution with hydrochloric acid; a brown oil separated out which was dissolved in acetone. After filtration, the acetone was distilled off and the oily residue was treated with several lots of boiling water. The combined aqueous extracts were treated with active carbon and filtered; crystals came out which were recrystallized until the m.p. was constant at 140-141°. m-N-Phenylaminobenzoic acid forms colorless prisms, readily soluble in ether and acetone, less readily soluble in benzene and alcohol. 0.9 g pure product was obtained, or 7% of the theoretical yield.

6.984 mg substance: 0.41 ml N_2 (15°, 742). 11.310 mg substance: 0.67 ml N_2 (15°, 742 mg). Found %: N 6.66, 6.71. $C_{13}H_{11}O_2N$. Calculated %: N 6.56.

Test of indicators. Indicator tests were performed with 0.001 N potassium bichromate, 0.001 M solutions of indicators prepared by dissolving 0.213 g p- and m-N-phenylaminobenzoic acids and 0.1 g sodium carbonate in 1 liter water. The total volume of the test solution was 100 ml. Following the earlier procedure [2] the following characteristics were determined: 1) limit of acidity (normality of sulfuric acid) at which the color of the indicator is sufficiently intense for titration; 2) minimum amount of indicator; 3) minimum amount of oxidizing agent; 4) stability and reversibility of the indicator. During the oxidation of p-N-phenylaminobenzoic acid the color changes from colorless through green to blue-violet. With m-N-phenylaminobenzoic acid the color changes from green to blue-violet through pink and the final color is weaker than that of the p-isomer. The results are given in the table.

When oxidation was performed with cerium sulfate a sufficiently intense color of the indicators is developed at a much lower acidity (in 2 N sulfuric acid). If excess of oxidizing agent is added to a solution containing ions of divalent iron, then the color of the indicators is developed at lower acidity. Consequently titration of Mohr's salt with both indicators is possible in 5-6 N sulfuric acid. The indicator error was determined by titrating solutions

of Mohr's salt with bichromate in presence of the new indicators side by side with titrations with diphenylaminesulfonic acid and phenylanthranilic acid. Identical results were obtained.

TABLE

Acid	p-Phenylaminobenzoic acid	m-Phenylaminobenzoic acid
oxidation-reduction potential	1.12 V	about 1.12V
acidity at which color is developed	3 N	2 N pale green
change of color with increased acidity	6.5 N pale violet	5.0 N develops pink color 6.5 N intense pink color 7.5 N pale violet color, rapidly changing to pink
limit of acidity	7.5 N optimum 9 N	9 N blue-violet color optimum 10 N
minimum of oxidizing agent in optimum conditions	1 ml optimum 2 ml	1 ml optimum 2 ml
minimum amount of indicator	1 ml	1.5 ml
color stability in optimum conditions	12 hours	1 hour

SUMMARY

1. p- and m-N-phenylaminobenzoic acids have been synthesized.

2. It is shown that the introduction of the carboxyl group into the diphenylamine molecule considerably increases the oxidation-reduction potential of the indicator, and the position of the carboxyl group hardly influences the oxidation-reduction potential.

3. m- and p-N-phenylaminobenzoic acids can be applied in titration with strong oxidizing agents such as bichromate and salts of tetravalent cerium.

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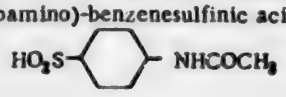
STUDIES ON QUINONES

I. REACTION OF p-BENZOQUINONE WITH ACYLAMINOSULFINIC ACIDS

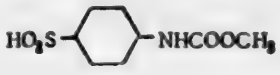
I. S. Ioffe

It is over 100 years since the discovery of p-benzoquinone by the "father of Russian chemistry", A. A. Voskresensky. This compound was the forerunner of a large group of quinones of great theoretical and practical importance. Among quinone derivatives we may include dyes, both natural and synthetic. Many natural organic compounds possessing physiological activity are also quinone derivatives.. Quinones have therefore attracted considerable attention and have been the object of numerous investigations. Nevertheless the reactions of these chemically very active compounds have not been exhausted. Descriptions of new quinone reactions are frequently appearing in the literature and many of these reactions have not been sufficiently developed. This is true of the reaction of quinone with sulfinic acids, described for the first time in 1894 by Ginsberg [1].

We have made a study of the products of reaction of p-benzoquinone with acylaminobenzenesulfinic acids, which are genetically related to sulfanilamide, in particular with p-acetylaminobenzenesulfinic acid (I) and p-(methoxycarbamino)-benzenesulfinic acid (II).



(I)

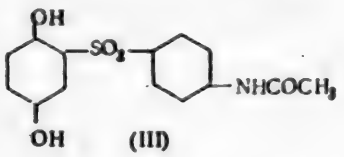


(II)

p-Acetylaminobenzene sulfinic acid [2] is prepared by reduction of p-acetylaminobenzene sulfochloride with sodium sulfite. In similar conditions, starting from the p-sulfochloride of methoxycarbaminobenzene (phenylurethylane), we prepared the previously undescribed sulfinic acid (II).

These sulfinic acids enter very quickly into reaction with p-benzoquinone. The resultant products are almost completely insoluble in hot water. We exploited this property in developing a very simple method for the nearly quantitative preparation of products of reaction of p-benzoquinone with the aforementioned sulfinic acids. To a boiling aqueous solution of the latter is added the finely pulverized quinone in small portions and with energetic stirring. Addition of each portion of quinone is marked by the appearance of a yellow color in the solution, but this disappears almost instantaneously and a colorless condensation product is precipitated.

Analyses and an examination of the properties of the products showed that they were formed by the addition to one molecule of quinone of one molecule of sulfinic acid (I) or (II). Such addition products contain an unchanged acylamino group and, as shown by quantitative acetylation, two hydroxyl groups. This proves that addition of sulfinic acids to the quinone takes place through the sulfinic groups with formation of 4-acylamino-2', 5'-dihydroxydiphenylsulfones with the structures (III) and (IV) respectively.



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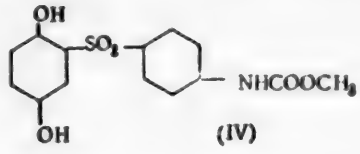


(IV)

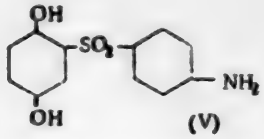
These compounds are probably formed by the scheme common to quinones:

with rearrangement of the product of addition into the hydroxy derivative (III) or (IV).

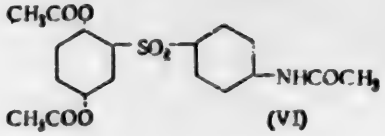
Quinones react according to this scheme with other compounds, for example, amines. In the majority of cases, however, the reaction does not stop at formation of the hydroquinone derivative, since the latter is oxidized by the original quinone with formation of still another new quinone derivative which is either precipitated or enters into reaction with a fresh molecule of the reaction component. The consequence is that the yield of condensation product does not exceed 50 or 33% (depending on the number of combining residues) of the amount of initial quinone;

In the condensation of quinone with sulfinic acids however, the reaction stops at the stage of formation of the hydroquinone derivative and the yield of this product approaches 100%. This difference in the course of reaction of quinone with sulfinic acids is explained, on the one hand, by the fact that the formed hydroquinone derivative is substantially insoluble in hot water and is precipitated, and, on the other hand, by the fact that quinone derivatives containing sulfone residues possess higher oxidation potentials than unsubstituted quinones. Thus, according to Fieser's data [3] in the α-naphthoquinone series the introduction of the tolylsulfonic residue raises the oxidation potential by 121 mV. Hence quinone derivatives containing sulfonic residues must possess stronger oxidizing properties than unsubstituted quinones. In the case under discussion, therefore, the quinone no longer oxidizes the hydroquinone derivatives (III) or (IV).

These two compounds differ in the character of the radical which acetylates the amino group. Their saponification yields one and the same amino compound, 4-amino-2', 5'-dihydroxydiphenylsulfone (V). The acetyl derivative (III) is readily saponified by both hydrochloric acid and caustic alkali. But the acyl derivative (IV) is not saponified by acid and remains unchanged even after prolonged boiling with hydrochloric acid; it is only saponified by alkali.



(V)



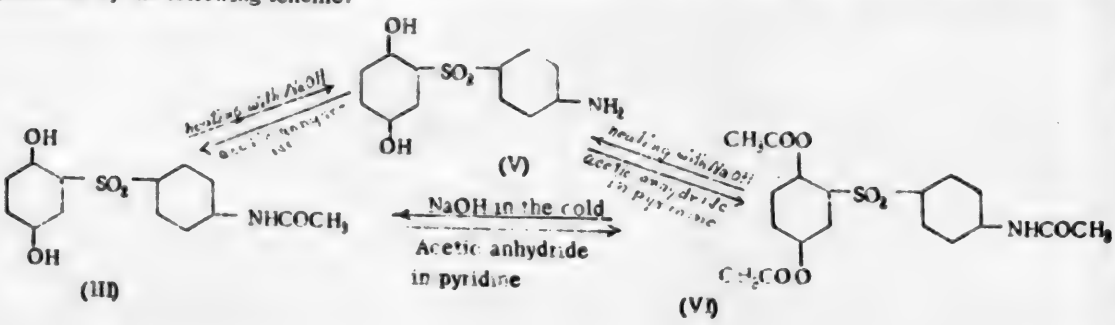
(VI)

The amino compound (V) is soluble in hot water. The best medium for crystallization of the compound is dilute alcohol. Colorless crystals are thus obtained with m.p. 175-176° which are soluble both in dilute caustic alkali and in dilute hydrochloric acid. The hydrochloride of 4-amino-2', 5'-dihydroxydiphenylsulfone is prepared by dissolving the amine in hot 10% hydrochloric acid and then cooling the solution. It comes down in the form of colorless crystals with m.p. 208-210°. The hydrochloride hydrolyzes in water with separation of the free amine.

Gentle heating of the amino compound with acetic anhydride leads to acetylation of only the amino group with formation of 4-acetylamino-2', 5'-dihydroxydiphenylsulfone (III), which forms colorless crystals, m.p. 282-285° identical with the product of condensation of quinone with acetylaminobenzene sulfinic acid. Acetylation with a mixture of acetic anhydride and pyridine leads to acetylation not only of the amino group but also of the hydroxy groups with formation of a triacetyl derivative (VI). In contrast to the monoacetyl derivative (III), the triacetyl derivative (VI) is soluble in hot alcohol; it crystallizes in the form of colorless crystals which melt at 180-182°. The same triacetyl derivative is obtained by acetylation with acetic anhydride in pyridine of the monoacetyl derivative (III).

The triacetyl derivative (VI) slowly goes into solution when treated with cold caustic alkali solution. During this operation only the acetoxy groups are saponified and acidification of the solution leads to precipitation of 4-acetamino-2',5'-dihydroxydiphenylsulfone. By heating with alkali the acetamino group is also saponified with formation of the amino compound (V).

The interrelations of 4-amino-2',5'-dihydroxydiphenylsulfone with its mono- and triacetyl derivatives may be represented by the following scheme:



EXPERIMENTAL

I. 4-Acetylamino-2',5'-dihydroxydiphenylsulfone (III).

a) Preparation. 20 g p-acetaminobenzenesulfinic acid is dissolved in 500 ml boiling water. The solution is filtered, again brought to the boil and addition is made, in small portions, of 11 g p-benzoquinone with good stirring. During the introduction of each portion of the quinone the solution turns orange-yellow, but this color vanishes almost at once. The solution rapidly begins to deposit the colorless condensation product, the quantity of which steadily increases. Toward the end of the experiment the quinone is added in extremely small portions. When at a certain moment the color does not disappear, addition is made to the suspension of a few milliliters of a solution of acetaminobenzenesulfinic acid until decolorization is complete. The suspension is then boiled for a further 15 minutes, after which the precipitate is filtered, washed on the filter with hot water, and dried. Yield 30 g, which is very close to the theoretical.

b) Properties. The compound is very poorly soluble in organic solvents, almost completely insoluble in water. It dissolves readily in dilute caustic alkali solutions with formation of a pale yellow solution which when acidified deposits the original compound in the form of slender, colorless needles (as viewed under the microscope). Heating of the alkaline solution causes saponification with formation of the amino compound. It also saponifies when heated with inorganic acids. It crystallizes from large volumes of acetic acid or alcohol in the form of colorless needles melting at 282-285° after darkening.

0.1322 g substance: 0.0978 g $BaSO_4$. 0.1622 g substance: 0.1214 g $BaSO_4$. Found %: S 10.20, 10.29. $C_{14}H_{13}O_5NS$. Calculated %: S 10.40.

Determination of hydroxyl groups by quantitative acetylation.

0.0030 g substance: 6.9 ml 0.1 N NaOH. 0.1246 g substance: 3.3 ml 0.1 N NaOH. Found %: OH 11.28, 11.32. $C_{14}H_{11}O_3NS(OH)_2$. Calculated %: OH 11.08.

II. 4-Acetylamino-2',5'-diacetoxydiphenylsulfone (VI).

a) Preparation. 3.1 g 4-acetoxy-2',5'-dihydroxydiphenylsulfone is introduced into a mixture of 40 g pyridine and 10 g acetic anhydride. The precipitate goes into solution when heated on the water bath. Heating on the water bath is continued for a further hour, after which the nearly colorless solution is poured into 300 ml hot water. On cooling, the acetylation product separates in the form of needles. These are filtered, washed with water and then crystallized from aqueous alcohol. Yield of crystalline substance 2.5 g or 64% of the theoretical.

b) Properties. The compound is highly soluble in hot water, alcohol and acetic acid. It crystallizes from slightly aqueous alcohol or from pure alcohol in the form of colorless, beautifully formed, slender needles. It melts sharply at 182-184°. It dissolves slowly in cold caustic alkali solution with saponification of the acetoxy groups. Acidification of this alkaline solution brings down 4-acetylamino-2',5'-dihydroxydiphenylsulfone with m.p. 282-285°. Heating with alkali causes saponification also of the acetamino group with formation of the amino compound.

0.1560 g substance: 0.0924 g $BaSO_4$. 0.1542 g substance: 0.0934 g $BaSO_4$. Found %: S 8.13, 8.3° $C_{16}H_{17}O_7NS$. Calculated %: S 8.18.

III. 4-Methoxycarbamino-2',5'-dihydroxydiphenylsulfone (IV).

a) Preparation. 22 g p-methoxycarbaminobenzenesulfinic acid, prepared by reaction of p-methoxycarbaminobenzenesulfochloride with sodium sulfite, is dissolved in 500 ml boiling water, and to the filtered solution is added, with boiling and good stirring, 11 g p-benzoquinone. The reaction proceeds as in that of quinone with p-acetylaminobenzenesulfinic acid. The reaction product, poorly soluble in hot water, comes out of solution. It is filtered, washed with hot water and dried. Yield 32 g or 97% of the theoretical.

b) Properties. Colorless crystals, poorly soluble in alcohol and acetic acid, sparingly soluble in hot water from which it crystallizes on cooling; m.p. 210-211°. Very stable when heated with inorganic acids and, unlike 4-acetylamino-2',5'-dihydroxydiphenylsulfone, is not saponified in these conditions. It only saponifies when heated with caustic alkalies.

0.1566 g substance: 0.1118 g $BaSO_4$. 0.1536 g substance: 0.1114 g $BaSO_4$. Found %: S 9.81, 9.96. $C_{14}H_{13}O_5NS$. Calculated %: S 9.91.

IV. 4-Amino-2',5'-dihydroxydiphenylsulfone (V).

a) Preparation by acid saponification of 4-acetamino-2',5'-dihydroxydiphenylsulfone. 30 g 4-acetamino-2',5'-dihydroxydiphenylsulfone is introduced into 150 ml 10% hydrochloric acid and the suspension is heated at the boil in a flask under a reflux condenser until the precipitate dissolves completely. The solution is evaporated

to dryness on the water bath. The dry precipitate is dissolved in 200 ml hot water to which is added a small quantity of hydrochloric acid, and the obtained solution is filtered after treatment with animal charcoal. The filtrate is stirred into a hot solution of 30 g sodium acetate in 200 ml water. The amino compound separates as colorless flocs which are stood for 12 hours and then filtered, washed with water and dried. Yield 22 g or 83% of the theoretical.

b) Preparation by alkaline saponification of 4-acetamino-2',5'-dihydroxydiphenylsulfone. 30 g 4-acetamino-2',5'-dihydroxydiphenylsulfone is dissolved in 150 ml 10% sodium hydroxide and the solution is brought to the boil. The completion of the reaction is recognized by the formation of a transparent solution when hydrochloric acid is added to a sample. Addition is then made to the reaction mass of 50 ml 20% acetic acid; after standing for 12 hours the amino compound comes down and is filtered, washed with water and dried. Yield 23 g or 85% of the theoretical.

c) Preparation by alkaline saponification of 4-methoxycarbamino-2'-5'-dihydroxydiphenylsulfone. 32 g of the methoxycarbamino compound is dissolved in 150 ml 10% sodium hydroxide and the saponification is conducted as in the preceding experiment. Yield of product the same.

d) Properties. Colorless crystalline substance. Readily soluble in alcohol and acetic acid; slightly soluble in hot water. Crystallizes nicely from aqueous alcohol on addition of traces of bisulfite. Melts with darkening at 175-176°. Forms a hydrochloride which crystallizes from 10% hydrochloric acid in the form of colorless crystals. Gentle heating with acetic anhydride converts it into 4-acetamino-2',5'-dihydroxydiphenylsulfone, separating as crystals with m.p. 282-285°. Heating with acetic anhydride in presence of pyridine converts it into 4-acetamino-2',5'-diacetoxydiphenylsulfone which melts at 180-182° after crystallization from aqueous alcohol. The compound is soluble in caustic alkalies, but the alkaline solutions gradually darken on standing. The aqueous solutions turn brown when treated with oxidizing agents and a brown precipitate is formed.

0.1344 g substance: 0.1188 g $BaSO_4$. 0.1120 g substance: 0.0980 g $BaSO_4$. Found %: S 12.14, 11.82. $C_{12}H_{11}O_4NS$. Calculated %: S 12.8.

e) Hydrochloride. Formed by dissolving the amino compound in hydrochloric acid. Crystallizes from 10% hydrochloric acid solution as colorless crystals, m.p. 208-210°. It is easily hydrolyzed in water from which the amino compound, m.p. 175-176°, comes down. The salt is stable when kept in a desiccator in the dry state.

SUMMARY

Reaction of p-benzoquinone with acylaminobenzenesulfinic acids yields colorless products of condensation of equimolar amounts of the starting components, possessing the structure of 4-acylamino-2',5'-dihydroxydiphenylsulfone. Saponification gives 4-amino-2',5'-dihydroxydiphenylsulfone. Mild acetylation of the latter leads to acetylation of only the amino group, but acetylation with acetic anhydride in pyridine leads to acetylation also of the hydroxy groups with formation of the triacetyl derivative – 4-acetylamino-2',5'-diacetoxydiphenylsulfone. Only the acetoxy groups are saponified by treatment with cold alkali solution. Full saponification occurs on heating with alkali and 4-amino-2',5'-dihydroxydiphenylsulfone is formed.

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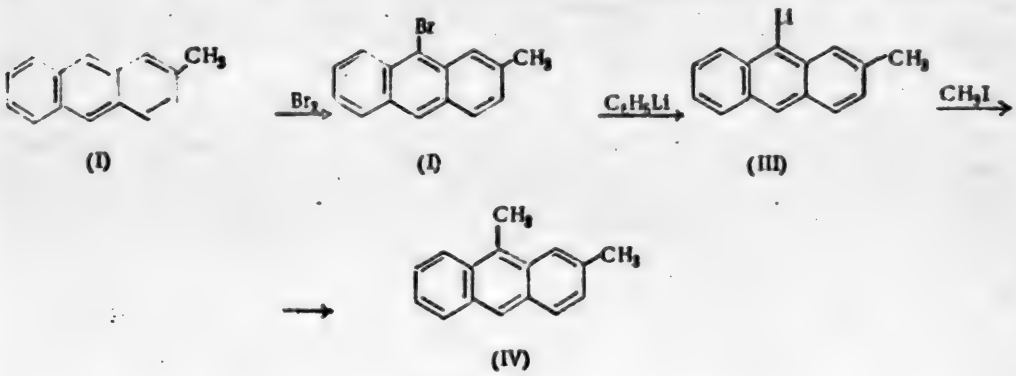
ORIENTATION PHENOMENA IN SUBSTITUTION REACTIONS WITH PARTICIPATION OF ORGANIC COMPOUNDS OF ALKALI METALS

B. M. Mikhailov and V.P. Bronovitskaya

With the aim of throwing light on the controversial question as to whether organic compounds of the alkali metals are to be regarded as electrophilic or nucleophilic reagents, we undertook a study of orientation phenomena in reactions with participation of bromine and phenyllithium in the anthracene series. Anthracene derivatives are convenient materials from the systematic standpoint.

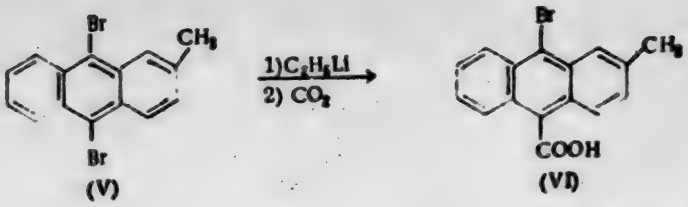
Starting materials were 2-methylanthracene and 2-methyl-9,10-dibromoanthracene. When one equivalent of bromine was reacted with a carbon bisulfide solution of 2-methylanthracene (I), one of two possible mesoisomers, 2-methyl-9-bromoanthracene (II), was separated in 63% yield, which fact permits the conclusion that substitution takes place mainly in the 9-position. The structure of the bromo compound (II) was established by its transformation into the dimethyl compound by replacing the bromine atom by lithium followed by reaction of the organolithium compound (III) with methyl iodide. The resultant hydrocarbon was 2,9-dimethylanthracene (IV), identical with the hydrocarbon formed by the Grignard reaction between methyl magnesium iodide and 2-methylanthrone-9:



(I) (II) (III) (IV)

Having established the orientating effect of a substituent of the first order in relation to the electrophilic reagent (bromine), we turned our attention to the second half of the problem – the elucidation of the direction of reaction with participation of an organometallic compound (phenyllithium). In this connection we did not study the hydrogen-lithium exchange reaction (metalation) – the usual procedure up to now – but the halogen-metal exchange reaction, and more precisely the action of phenyllithium on 2-methyl-9,10-dibromoanthracene. Our selection of this type of reaction was influenced by the consideration that replacement of hydrogen atoms by bromine in the 2-methylanthracene molecule does not change the relative electro-negativity of the meso carbon atoms and consequently does not reflect the direction of reaction with the organometallic reagent, whereas replacement of halogen by metal proceeds more quickly and completely and is not complicated by intermediate reactions as is the case with metalation when, for example, toluene is first metalated at the methyl group and subsequent metalation in the ring is governed not by the methyl group but by the methyl-metal group.

Reaction of one equivalent of phenyllithium with 2-methyl-9,10-dibromoanthracene (V) followed by hydrolysis of the formed isomeric organolithium compounds gave one of the two possible isomers, 2-methyl-9-bromoanthracene (II), but the low yield (24%) did not permit a decision as to whether the preferred course of the halogen-metal exchange reaction was at the 9- or the 10- position. The products of reaction of phenyllithium with 2-methyl-9,10-dibromoanthracene were then subjected to carboxylation, and from the obtained carboxylic acids we were able to isolate an acid (m.p. 238°) in the pure form in a yield of 59% of the theoretical. This acid proved to have the structure of 2-methyl-9-bromoanthracene-10-carboxylic acid (VI). This structure was established by comparison with a specimen of the isomeric acid, 2-methyl-10-bromoanthracene-10-carboxylic acid (VIII).

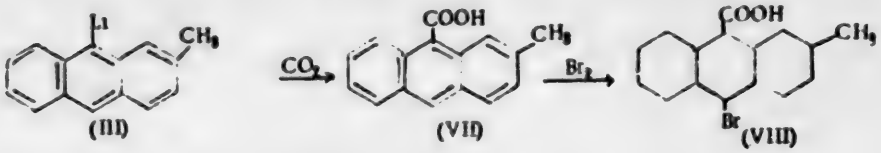


(V) (VI)

The latter was prepared by the following series of transformations which left no doubt about its structure.

Treatment of 2-methyl-9-bromoanthracene (II) with n-butyllithium gave the organolithium compound (III); carboxylation of the latter gave 2-methylanthracene-9-carboxylic acid (VII), which was converted by bromination into acid (VIII) with m.p. 230 5°. The position of the bromine in the ac . was confirmed by oxidation to 2-methylanthraquinone.

A mixed sample of acid (VI) and (VIII), whose melting points are fairly close, had a lower melting point.



(III) (VII) (VIII)

Hence the action of phenyllithium on 2-methyl-9, 10-dibromoanthracene is marked by preferential substitution by lithium of the bromine atom in the 10-position, i.e., the methyl group manifests an opposite orientating influence in substitution reactions with participation of organometallic and electrophilic reagents. From this it follows that organometallic compounds should be regarded not as electrophilic reagents (Morton) but as compounds which in course of reaction suffer breakdown into radicals and which function as nucleophilic reagents, in the same manner as metallic sodium [1], due to a tendency of the metal atom to change into a cation.

The theory of the nature of organometallic reagents here propounded is in direct contradiction to the theories enunciated in the literature [2].

Various concepts of the character of organometallic reagents have been advanced because the problem of orientation with their participation is a complex one, and the whole of the experimental material relating to the reactions does not fit into the framework of any single substitution scheme, and gives occasion to regard organometallic compounds sometimes as nucleophilic reagents and in other cases as electrophilic ones. For example, fluorobenzene and triphenylamine, which contain ortho-para-orientating substituents in respect of electrophilic reagents, are metalated differently: fluorobenzene in the ortho-position and triphenylamine in the meta-position.

The totality of conflicting phenomena of substitution in metalation processes can be reconciled and systematized if we assume that in the final organometallic compounds containing alkali metal in the ortho-position to an electronegative substituent, as for example in o-lithium-fluorobenzene, there is effected a bond between metal and heteroatom similar in character to the hydrogen bond. Formation of a hydrogen-like bond between metal and heteroatom energetically stabilizes the system and is therefore a thermodynamic factor promoting the substitution reaction in the ortho position.

The theory propounded above appears entirely plausible if we consider that, first, the distance between the alkali metal and the heteroatom when in the ortho-position to each other, for example in o-lithium-fluorobenzene or o-lithium-anisole, is of the same order (2.75 A) as in compounds containing a typical hydrogen bond (2.25-3 A), and second organic compounds of alkali metals tend to form complexes [3]. The justification for postulating the occurrence of a hydrogen-like interaction between the alkali metal and the atom of the electronegative element is founded on the totality of metalation reactions of variously constituted aromatic and heterogeneous compounds. A comparison of the factual material relating to this field of transformations leaves no doubt also that in cases when the reaction course is not complicated by the supplementary effects of hydrogen-like interactions of the substituents the organometallic compounds behave unmistakably like nucleophilic reagents.

Indeed in compounds with ortho- and para-orientations which are electropositive (in phenyllithium and benzylsodium) or weakly electronegative (in triphenylamine, triphenylarsine and triphenylphosphine) metalation takes place in the meta-position. In all compounds, however, with strongly electronegative substituents capable of entering into reaction with alkali metals, substitution takes place in the ortho-position.

Compounds of the latter type fall into two groups. First, we have compounds containing ortho- and para-directive substituents and undergoing substitution under the action of both electrophilic and organometallic reagents in the ortho-position, and therefore justifying the classification of organic compounds of the alkali metals as electrophilic reagents. Examples are fluorobenzene, aniline, sodium phenolate, anisole, furane, thiophene and a series of other compounds.

The second group will include representatives of the benzene, diphenyl and heterocyclic series. In these no consistency of orientation is observed when using electrophilic and metalating reagents. In this group of compounds substitution under the action of the latter reagents likewise takes place in the ortho-position to the heteroatom.

As examples we may cite the transformations of diphenyl ether (metalation in the 2-position [4], halogenation in the 4-position [5]) dibenzofuran (metalation in the 1-position [6,4], halogenation in the 3-position [7,8]) and many other compounds.

EXPERIMENTAL

2-Methylanthracene. 5 g 2-methylanthraquinone, 4.5 g granulated tin and 34 ml glacial acetic acid are heated to boiling in a flask under a reflux condenser. Addition is made to the boiling solution over a period of two hours of 12.5 ml concentrated hydrochloric acid (spgr1.19) in 1 ml portions. The reaction mass is then diluted with 50 ml water and the yellow precipitate is filtered off.

A mixture of the prepared methylanthrone, 6 g zinc dust and 100 ml 2 N NaOH was boiled for 3 hours. The precipitate was filtered and treated with 10% hydrochloric acid for removal of unreacted zinc dust. The obtained hydrocarbon was crystallized from benzene-alcohol. M.p. 208-209°. Yield 72.7%.

2-Methylanthracene has previously been prepared by reduction of 2-methylanthraquinone with zinc dust and ammonia [9] or by heating with zinc dust at high temperature [10]; yields not specified, m.p. 207°.

2-Methyl-9-bromoanthracene:

a) To a carbon bisulfide solution (75 ml) of 3 g 2-methylanthracene (cooled to 0°) in a three-necked flask fitted with mechanical stirrer, reflux condenser and dropping funnel, was added very slowly and with energetic stirring a carbon bisulfide solution (15 ml) of 2.5 g bromine. The reaction mass was then stirred on the water bath until hydrogen bromide ceased to be evolved; the solvent was then distilled off and the residue crystallized from alcohol.

There was obtained 2.8 g of a substance with m.p. 84-91°; a less pure fraction was recovered from the partially concentrated nother liquor, and after crystallization from dioxane-alcohol it melted at 91-94° (0.36 g). The yield of bromo compound melting over a three degree range was equal to 63%.

After recrystallization from alcohol, 2-methyl-9-bromoanthracene formed yellow, transparent rhombic platelets with m.p. 94.5-95.5°.

4.979 mg substance: 12.106 mg CO_2; 1.757 mg H_2O. Found %: C 66.35; H 3.94. $C_{15}H_{11}Br$. Calculated %: C 66.42; H 4.09.

b) To a solution of phenyllithium(0.0058 mole) was introduced slowly 2 g 2-methyl-9,10-dibromoanthracene (m.p. 141-142° [11]). At the end of 30 minutes the organolithium compound was hydrolyzed with an ethereal solution of methanol, the reaction mixture was washed with water, the ether driven off and the residue (1.63 g) crystallized from alcohol. There was obtained 0.52 g substance with m.p. 82-87°, this was crystallized from 1:1 dioxane-alcohol to give 0.24 g with m.p. 93-95° and 0.12 g with m.p. 88-91° in the form of yellow platelets. Yield 24% of the theoretical. The melting point of a mixture of the compound melting at 93-95° with 2-methyl-9-bromoanthracene prepared by bromination of 2-methylanthracene was not depressed.

From the evaporated mother liquor, after separation of a fraction weighing 0.52 g, there was isolated 0.81 g of a low melting mixture of bromo compounds with m.p. 44-52°. Chromatography on alumina followed by crystallization from alcohol-ether gave a product with m.p. 43-53° which was found by analysis to be a mixture of the isomeric 2-methyl-9-bromo- and 2-methyl-10-bromoanthracenes.

6.077 mg substance: 14.764 mg CO_2; 2.148 mg H_2O. Found %: C 66.31; H 3.95. $C_{15}H_{11}Br$. Calculated %: C 66.42; H 4.09.

2,9-Dimethylanthracene. To an ethereal solution of phenyllithium (0.0037 mole) was added 1 g 2-methyl-9-bromoanthracene. At the end of 30 minutes addition was made of an ethereal solution of 1.58 g methyl iodide which reacted with the organolithium compound with considerable heat development. After holding for 30 minutes at room temperature, the reaction products were washed with water, the ether was driven off, and the residue (0.89 g) was crystallized from methanol.

There was obtained 0.28 g yellow crystalline substance with m.p. 81-82°; the mother liquor yielded a further 0.25 g with m.p. 79-82°. Yield 69.7% of the theoretical. The melting point of a mixture of the compound melting at 81-82° with 2,9-dimethylanthracene prepared by reacting 2-methyl-9-anthrone with methyl magnesium iodide [12] (m.p. 80.5-82°) was not depressed.

2-Methylanthracene-9-carboxylic acid. To a solution of n-butyllithium, prepared from 1.42 g n-butyl chloride, 0.21 g lithium and 30 ml ether, was added 2 g 2-methyl-9-bromoanthracene. After a period of 30 minutes the reaction mixture was carboxylated by pouring on to solid carbon dioxide. Crystallization of the acidic reaction products from dilute (50%) alcohol gave 10.5 g yellow crystals with m.p. 187-189°. Further crystallization of the acid from benzene gave 0.9 g substance with m.p. 197-198° in the form of light-yellow needlets. Yield equal to 51.7% of the theoretical.

4.825 g substance: 14.424 mg CO_2; 2.216 mg H_2O. Found %: C 81.58; H 5.13. $C_{16}H_{12}O_2$. Calculated %: C 81.33; H 5.12.

Judging by the melting point, the acid of unestablished structure (m.p. 197°) obtained by Liebermann [11,13] by the action of oxalyl chloride on 2-methylanthracene is 2-methylanthracene-9-carboxylic acid.

2-Methyl-10-bromoanthracene-9-carboxylic acid. To a suspension (cooled to 0°) of 0.9 g 2-methylanthracene-9-carboxylic acid in 15 ml carbon disulfide was slowly added, with stirring, a solution of 0.63 g bromine in 10 ml carbon bisulfide. When all the bromine had been added, the reaction mixture (a brown suspension) was heated on the water bath until hydrogen bromide ceased to come off; the solvent was then distilled off and the residue crystallized from dilute alcohol.

There was obtained 0.86 g substance with m.p. 205-213° (with decomp.). Crystallization from benzene gave 0.6 g (50% of the theoretical yield) of acid with m.p. 223.5-225° in the form of yellow needles. One more crystallization from benzene gave a melting point of 229-230.5°. A mixture of the acid with 2-methyl-9-bromoanthracene-10-carboxylic acid of m.p. 235-238°, prepared from 2-methyl-9,10-dibromoanthracene, melted at 217-233°.

5.505 mg substance: 12.205 mg CO_2; 1.734 mg H_2O. Found %: C 60.71; H 3.52. $C_{16}H_{11}O_2Br$. Calculated %: C 60.95; H 3.52.

Oxidation of 2-methyl-10-bromoanthracene-9-carboxylic acid. To a solution of 0.2 g 2-methyl-10-bromoanthracene-9-carboxylic acid in acetic acid, heated on the water bath, was added an acetic acid solution of 0.17 g chromic oxide. The reaction mixture was left for 18 hours at room temperature, after which the acetic acid was distilled off and the residue was washed with water and crystallized from alcohol. There was obtained 0.08 g nearly colorless slender needles (57% of theory) with m.p. 163-167°.

The melting point rose to 171-174° after crystallization from dilute acetic acid, and there was no depression of melting point in admixture with a specimen of 2-methylanthraquinone (m.p. 173-174°).

2-Methyl-9-bromoanthracene-10-carboxylic acid. To a solution of 3 g 2-methyl-9,10-dibromoanthracene in 20 ml absolute benzene was added an ethereal solution (11.8 ml) of 0.729 g phenyllithium. After the lapse of 30 minutes the reaction mixture was carboxylated by pouring on to solid carbon dioxide.

The acidic reaction product (2.68 g with m.p. 216-221°) was crystallized from dilute (50%) alcohol to give 1.59 g acid in the form of yellow needlets with m.p. 235-238° (with decomp.). Yield equal to 59% of the theoretical.

4.510 mg substance: 10.054 mg CO_2; 1.516 mg H_2O. Found %: C 60.84; H 3.76. $C_{16}H_{11}O_2Br$. Calculated %: C 60.95; H 3.52.

SUMMARY

1. The hydrogen atom in position 9 is substituted by bromine when one equivalent of bromine acts on 2-methylanthracene.

2. One equivalent of phenyllithium reacts with 2-methyl-9,10-dibromoanthracene with substitution of a halogen by lithium, preferentially in the 10-position.

3. Organic compounds of alkali metals are nucleophilic reagents.

4. In organometallic compounds of an alkali metal present in the ortho-position to the electronegative substituent, a bond is developed between the metal and the heteroatom which is similar in character to the hydrogen bond. This bond is the factor governing the orientation during metalation.

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SYNTHESIS OF THE SIMPLEST CYANINES

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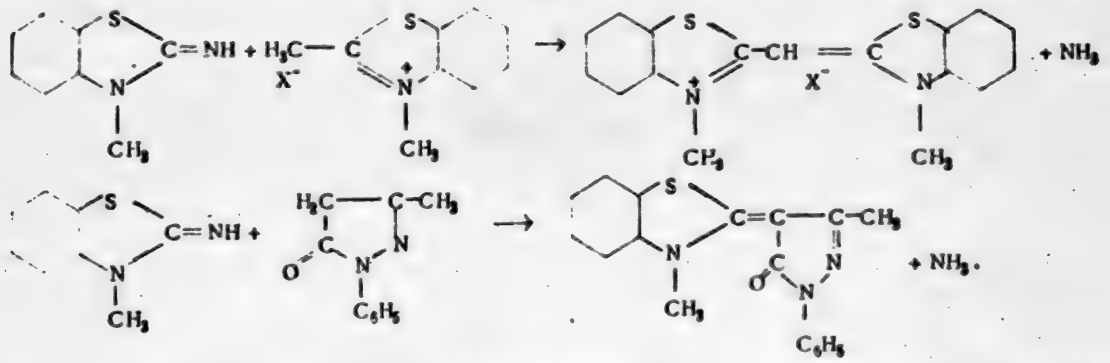
G. M. Oksengendler and A. I. Kiprianov recently showed [1] that auramine and the methylmethosulfate of Michler's thioketone are more susceptible to condensations with compounds containing active methyl or methylene groups than is Michler's ketone itself.

If we compare the derivatives of Michler's ketone, each with a carbonyl group, with the same derivatives of N-methylbenzothiazole, we can detect a profound similarity in their structure and properties. Thus, to Michler's ketone corresponds N-alkylbenzothiazolone; as we know, the latter compound is incapable of entering into a condensation reaction and Michler's ketone condenses with difficulty. To Michler's thioketone corresponds N-methylbenzothiazolonethione. Both compounds are nonreactive; however, the products of addition of dimethyl sulfate to these substances (the methylmethosulfate of Michler's thioketone and the methylmethosulfate of 2-methylmercaptobenzothiazole) are extremely reactive compounds. Finally, to auramine corresponds N-methylbenzothiazoloneimine.

On the basis of this analogy we suggested, and then demonstrated experimentally, that N-alkylbenzothiazoloneimines are also capable of condensing with heterocyclic compounds containing active methyl or methylene groups.

By short-period heating to 180-190° of heterocyclic bases with quaternary salts we have prepared monomethinecyanines, while with substances containing the $-CH_2-CO-$ group (of the type of methylphenylpyrazolone) we prepared merocyanines (without a polymethine chain). The reactions proceed according to the equations:



The yield of monomethinecyanines is 60-70% of the theoretical, and that of merocyanines is 80-90%. These reactions do not take place in solvents (acetic anhydride, pyridine).

Merocyanines can also be obtained with N-ethyl-2-pyridonimine, but in low yield.

Several methods are now known for the preparation of monomethinecyanines and merocyanines (without a polymethine chain). The most widely applied of these is based on the reactivity of alkyl- or arylmercapto groups situated in the α- or γ-position to the quaternary heterocyclic nitrogen.

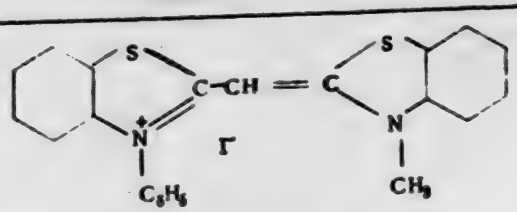
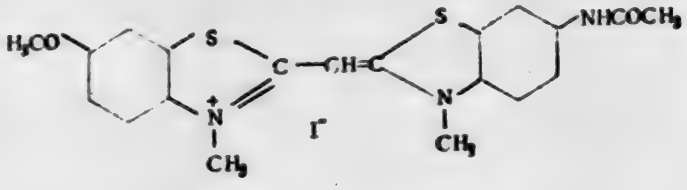
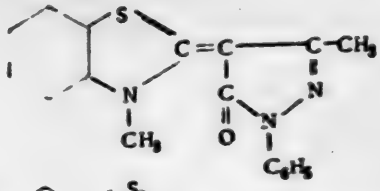
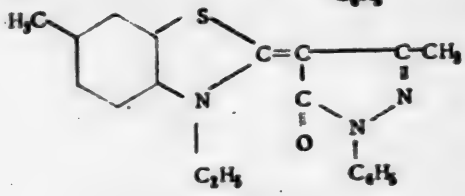
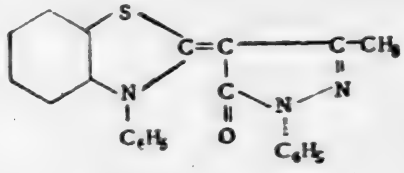
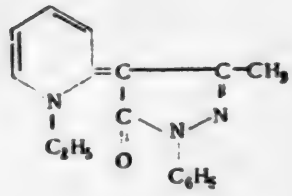
Other methods, based on utilization of quaternary salts containing a reactive iodine atom or a cyano group, have limited applicability.

The method of preparation of monomethinecyanines with the help of amyl nitrite in acetic anhydride may be adapted to reactions with an active cyano group.

The first method of preparation of monomethinecyanines reported in the literature—condensation of quinone- and quinaldine-alkyl iodides in presence of potassium hydroxide—is today of limited use.

The methods proposed by us for preparation of monomethinecyanines and merocyanines offer definite

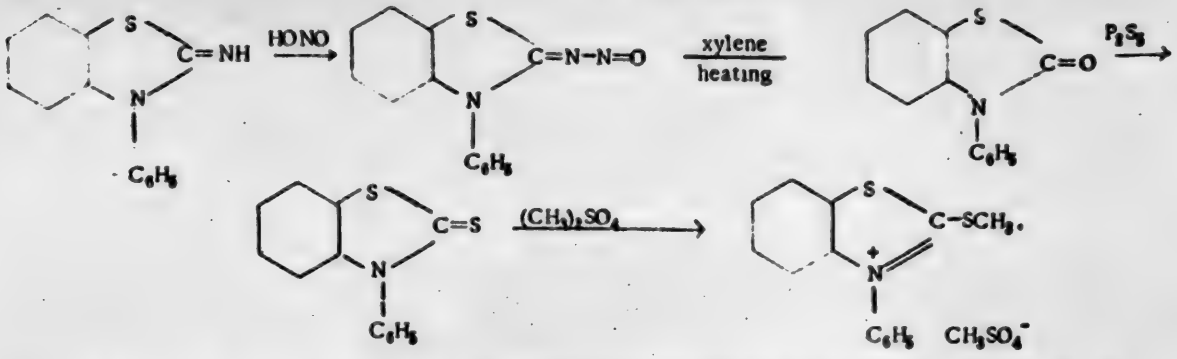
TABLE

Preparation No.	Formula	Melting point (corr)
(I)		278°
(II)		290
(III)		177
(IV)		143
(V)		280
(VI)		185

advantages over known methods of synthesis of these dyes if we exclude the simplest compounds prepared from 2-mercaptobenzothiazole. Actually, derivatives of 2-benzothiazoloneimine are more accessible compounds than the quaternary salts of the corresponding 2-alkylmercapto derivatives usually employed for the synthesis of dyes.

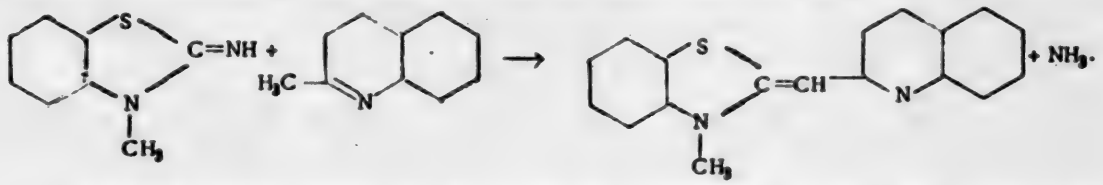
Thus, thiocyanation of p-anisidine readily yields 2-amino-6-methoxybenzothiazole, from which is obtained the N-alkyl-6-methoxybenzothiazoloneimines, whereas 2-mercapto-6-methoxybenzothiazole can only be prepared from the corresponding o-aminothiophenol by the action of carbon bisulfide [2].

The synthesis of monomethinecyanines and merocyanines of the benzothiazole series, containing aryl groups at the heterocyclic nitrogen, requires salts of 3-aryl-2-methylmercaptobenzothiazolium. These can be prepared only from the corresponding imines according to the scheme [3]:



If, however, we make direct use of N-arylbenzothiazoloneimines for the preparation of dyes, then four stages can be omitted. From N-phenylbenzothiazoloneimine we have prepared monomethinecyanine in 60% of the theoretical yield and merocyanine in 90% of the theoretical yield.

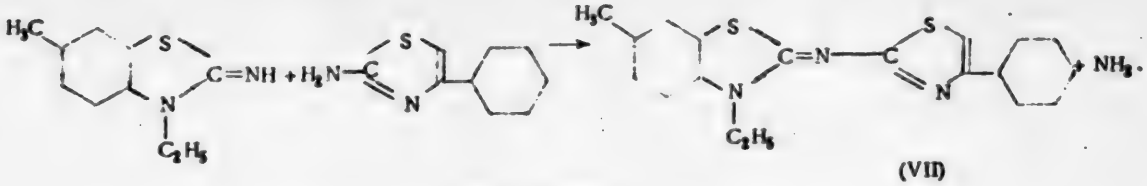
We only found one reference in the literature to a similar condensation. In 1936 Clark [4] prepared the base of pseudothiacyanine by condensation of N-methylbenzothiazoloneimine with quinaldine:



α- and β-2-methylnaphthothiazoles do not enter into reaction with α-picoline. Being limited to this sole example of the condensation of benzothiazoloneimine, Clark was unable to demonstrate the general character of this reaction and the possibility of utilizing benzothiazoloneimines for the preparation of the simplest cyanines.

In the table are listed the monomethinecyanines and merocyanines prepared by us and not described in the literature.

N-Alkylbenzothiazoloneimines can also be used for synthesis of azacyanines. Thus, azacyanine base (VII) is readily prepared by fusing N-ethyl-6-methylbenzothiazoloneimine with 2-amino-4-phenylthiazole.



(VII)

EXPERIMENTAL

2-Amino-4-phenylthiazole is prepared from acetophenone and thiourea with addition of bromine [5].

2-Amino-6-methoxybenzothiazole is prepared by thiocyanation of p-anisidine [6].

6-Methyl-N-ethylbenzothiazoloneimine is prepared from 2-amino-6-methylbenzothiazole by heating with ethyl iodide and subsequent treatment with caustic alkali [7].

N-Methylbenzothiazoloneimine. 1.5 g 2-aminobenzothiazole and 1.9 g methyl ester of p-toluenesulfonic acid were fused over a bare flame until a homogeneous melt was obtained, and then heated for 20 minutes at 140-150°. The reaction product was dissolved in 20 ml water (the whole dissolved) and into the still warm solution was run, gradually, while rubbing with a glass rod, a solution of 1.3 g potassium hydroxide in 5 ml water. The imine came down in the form of lustrous crystals. On the following day the crystals were drained, washed with cold water and dried. Yield 1.2 g (73% of the theoretical); m.p. 124°. Hunter [8] gives m.p. 123°.

6-Methoxy-N-methylbenzothiazoloneimine. Prepared from 1.8 g 2-amino-6-methoxybenzothiazole and 2 g methyl ester of p-toluenesulfonic acid by the preceding procedure. The oily layer which separated on addition of the alkali was twice extracted with hot benzene, the benzene was distilled off and the residue of benzene was removed in a drying cupboard. Yield of crude imine 1.5 g (77% of theoretical). After crystallization from ligroin it forms colorless needles with m.p. 94° (corr.). Not described in the literature.

Found %: N 14.3, 14.4. $C_9H_{10}ON_2S$. Calculated %: N 14.43.

The mother liquors obtained after recrystallization of the imine from ligroin were shaken with concentrated hydrochloric acid in a separating funnel to form the hydrochloride; after recrystallization from dilute hydrochloric acid it had m.p. 320° (corr.).

Found %: N 12.10. Cl 15.15. $C_9H_{11}ON_2SCl$. Calculated %: N 12.14; Cl 15.4.

N-phenylbenzothiazoloneimine was prepared from N,N'-diphenylthiourea by treatment with bromine in chloroform solution [8].

3,3'-Dimethylcyanine iodide. 0.5 g N-methylbenzothiazoloneimine and 1 g methylmethosulfate of 2-methylbenzothiazole were pulverized together and then fused in vacuum for 15 minutes at 180-190°. Toward the end of the reaction the melt began to foam and solidified. The reaction product was dissolved in 30 ml alcohol, water was added until turbid, and the hot solution was filtered. The filtrate was heated and 5 ml acetone was added, followed by a solution of potassium iodide (3 g) in water (10 ml); the precipitated dye was filtered, washed with acetone, water, and again acetone. Yield of crude product (straw-colored silky needles) 0.86 g (66% of the theoretical). M.p. 304° after recrystallization from alcohol; does not depress the melting point of monomethinecyanine prepared from the methoiodides of 2-methylmercaptobenzothiazole and 2-methylbenzothiazole.

Found %: N 6.24; I 29.02. $C_{17}H_{15}N_2S_2I$. Calculated %: N 6.39; I 28.99.

3-Phenyl-3-methylthiacyanine-iodide (I). Prepared from 1.13 g N-phenylbenzothiazoloneimine and 1.38 g methosulfate of 2-methylbenzothiazole by the previous method. Yield of crude product (yellow silky needles) 1.5 g (60% of the theoretical); recrystallization from alcohol gave 1.35 g with m.p. 278°.

Found %: I 25.32. $C_{22}H_{17}N_2S_2I$. Calculated %: I 25.40.

(6-Methoxy-3-methyl)-(6'-acetylamino-3'-methyl)-thiacyanine iodide (II). 0.4 g 6-methoxy-N-methylbenzothiazoloneimine and 0.66 g methylmethosulfate of 6-acetylaminobenzothiazole were fused and worked up as before. Yield of crude product 0.7 g (68% of the theoretical). Yellow crystalline powder, after recrystallization from alcohol; m.p. 290°.

Found %: N 8.0. $C_{20}H_{20}O_2N_3S_2I$. Calculated %: N 8.01.

4-[3'-Methyl-6'-methoxybenzothiazolinylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone], (III). 0.87 g 1-phenyl-3-methyl-5-pyrazolone was fused with 0.97 g 6-methoxy-N-methylbenzothiazoloneimine at 150-155° for 2 hours in vacuum (10-15 mm). The reaction product was dissolved with heating in alcohol, the solution was filtered, and water was added to the hot filtrate until turbid. An oil separated after standing overnight. The solution was poured off and heated, and again water was added until turbid. Beautiful yellow needles separated. The mother liquor was used for crystallization of the initially separated oil. The dye was again crystallized from ligroin M.p. 177°. Total yield 1.5 g (90% of the theoretical).

Found %: N 11.84, 11.74. $C_{19}H_{17}O_2N_3S$. Calculated %: N 11.96.

4-[3'-Ethyl-6-methylbenzothiazolinylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone] (IV). 0.87 g 1-phenyl-3-methyl-5-pyrazolone was fused with 0.96 g 6-methylbenzothiazoloneimine as in the preceding experiment, until ammonia ceased to come off. After recrystallization from aqueous alcohol, there was obtained 1.2 g (69% of the theoretical) of yellow prisms melting at 143°.

Found %: N 11.99, 11.85. $C_{20}H_{19}ON_3S$. Calculated %: N 12.03.

4-[3'-Phenylbenzothiazolinylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone] (V). Preparation as for (III), from 1.12 g N-phenylbenzothiazoloneimine and 0.88 g methylphenylpyrazolone. Fusion in vacuum was performed during 10 minutes at 170-180°. After crystallization from alcohol there was obtained 1.765 g (92% of the theoretical) of yellow needles. After recrystallization from toluene the m.p. was 280°.

Found %: N 10.87, 10.82. $C_{13}H_{17}ON_3S$. Calculated %: N 10.96.

4-[1'-Ethyldihydropyridylidene-(2')]-[1-phenyl-3-methyl-5-pyrazolone] (VI). 0.94 g 2-aminopyridine was fused with 2 g ethyl ester of p-toluenesulfonic acid at 130-140° for 20 minutes. The quaternary salt was dissolved in a little water, 1 g sodium hydroxide was added, and the pyridonimine three times extracted with small quantities of benzene. The benzene was distilled off and to the residual oil (0.9 g) was added 1.75 g methylphenylpyrazolone. Heating was effected at 150-160° in vacuum (30-40 mm) for 3 hours. Yellow needles with m.p. 185° were obtained by recrystallization from alcohol. Yield 0.14 g (5% of the theoretical).

Found %: N 14.88, 15.06. $C_{17}H_{17}ON_3$. Calculated %: N 15.05.

[3-Ethyl-6-methylbenzothiazolinylidene-(2)]-[2-amino-4-phenylthiazole] (VII). 0.96 g N-ethyl-6-methylbenzothiazoloneimine and 0.88 g 2-amino-4-phenylthiazole were fused at 165-170° in vacuum until ammonia ceased to come off. The yield of crude azacyanine base was 0.98 g (56% of the theoretical). After two crystallizations from alcohol the m.p. was constant at 186° (corr.). Nearly colorless, rhombic platelets.

Found %: N 12.00, 12.14. $C_{19}H_{17}N_3S_2$. Calculated %: N 11.94.

SUMMARY

1. A synthesis is proposed for the simplest cyanines, based on the ability of alkylbenzothiazoloneimines to enter into condensation with heterocyclic compounds containing an active methyl, methylene or amino group.

2. 7 dyes (the simplest cyanines) were synthesized by this method.

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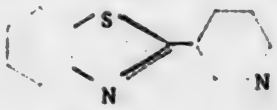
CONDENSATION OF o-AMINOTHIOPHENOL WITH HETEROCYCLIC CARBOXYLIC ACIDS

I. PYRIDYLBENZOTHIAZOLES

V. M. Zubarovsky and A. I. Voronina

The condensation of o-aminothiophenol with carboxylic acids of the heterocyclic series has not been investigated. This reaction can serve as a method of synthesis of benzothiazole derivatives containing various heterocycles in the 2-position; benzothiazoles of this type have not been investigated; a few of them are known. We have performed the condensation of o-aminothiophenol with the monobasic pyridine-carboxylic acids: picolinic, nicotinic and isonicotinic. The following isomeric pyridylbenzothiazoles were isolated: 2-[pyridyl-(α)]-benzothiazole (I), 2-[pyridyl-(β)]-benzothiazole (II), and 2-[pyridyl-(γ)]-benzothiazole (III).

(I)



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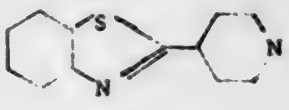
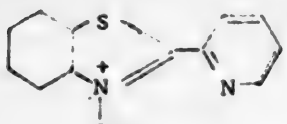


(III)

Condensation of o-aminothiophenol with the pyridinecarboxylic acids was effected by the usual method: heating of equimolar amounts of the starting components in sealed glass tubes. The condensation reaction is accompanied by a decarboxylation of the pyridinecarboxylic acids, and this is apparently the cause of the low yields (33-35%) of pyridylbenzothiazoles (I) and (II) obtained from picolinic and nicotinic acids. An attempt to replace nicotinic acid by its ethyl ester was unsuccessful, for the ester did not react with o-aminothiophenol after heating for 5 hours at 200°. The pyridylbenzothiazoles (I) and (II) are formed with higher yield (60%) by reacting o-aminothiophenol with the chlorides of picolinic and nicotinic acids. In the conditions of condensation with o-aminothiophenol, isonicotinic acid is less easily decarboxylated and 2-[pyridyl-(γ)]-benzothiazole is therefore obtained in a yield of 65%.

The isomeric pyridylbenzothiazoles possess basic character to extents depending on the mode of addition of the pyridine to the benzothiazole residue. Interest is attached to the mutual influence of these residues. 2-[Pyridyl-(α)]-benzothiazole is a very weak base: in dilute hydrochloric acid it does not dissolve without heating; in concentrated acid it dissolves in the cold but the salt formed in solution slowly hydrolyzes when excess of water is added; this pyridylbenzothiazole does not react with alkyl halides. One of its quaternary salts, 3-methyl-2-[pyridyl-(α)]-benzothiazole iodide (IV), was prepared by the action of the picolinic acid halide on o-methyl-aminothiophenol.



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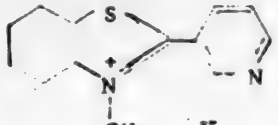

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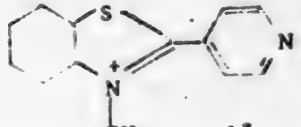
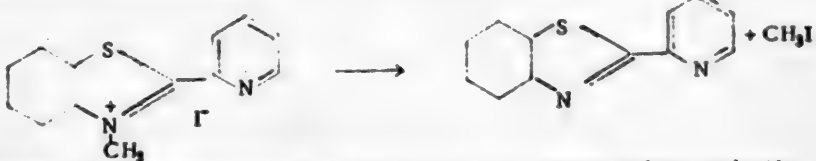


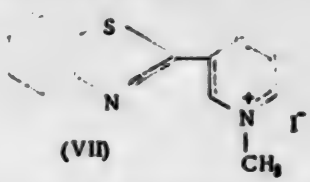
(VI)

This quaternary salt decomposes, however, when heated and is quantitatively transformed into methyl iodide and 2-[pyridyl-(α)]-benzothiazole:

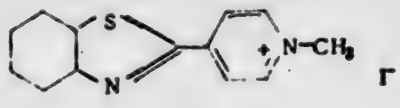


In contrast to 2,2'-dibenzothiazole which dissolves in concentrated sulfuric acid with a characteristic intense yellow color [1], 2-[pyridyl-(α)]-benzothiazole dissolves with a very weak yellow color. With divalent iron, 2-[pyridyl-(α)]-benzothiazole, like 2-[pyridyl-(α)]-quinoline [2], does not form a colored complex cation;

in this respect both of these compounds differ markedly from α,α'-dipyridyl, although their structures are similar. 2-[Pyridyl-(β)]-benzothiazole dissolves in concentrated sulfuric acid to form a nearly colorless solution. 2-[Pyridyl-(α)]-benzothiazole, on the other hand, is a fairly strong base; it dissolves in dilute hydrochloric acid with evolution of heat and forms a stable salt which can be isolated. It forms quaternary salts with alkyl halides. Analysis of these salts shows that 2-[pyridyl-(β)]benzothiazole is a monoacidic base; salt formation proceeds at the expense of the pyridine residue, since it forms the compound (VII) with methyl iodide and this compound is not identical with the 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide (V) synthesized from o-methylaminothiophenol and nicotinic acid halide.



(VII)



(VIII)

The basic properties of the pyridine residue are so weakened in 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide that this compound does not react when heated with excess of methyl iodide. Heating to the melting point leads to isomerization:

(VII)

3-Ethyl-2-[pyridyl-(β)]-benzothiazolium iodide is also isomerized by the same method.

2-Pyridyl-(γ)]-benzothiazole unexpectedly proved to be closer in basic properties to 2-[pyridyl-(β)]-benzothiazole than to 2-[pyridyl-(α)]-benzothiazole. Qualitative tests indicate the 2-[pyridyl-(γ)]-benzothiazole is a somewhat weaker base than 2-[pyridyl-(β)]-benzothiazole, at least in relation to dilute hydrochloric acid; regarding the reactions with alkyl halides, both of these bases behave very similarly. 2-[Pyridyl-(γ)]-3-methyl-benzothiazolium iodide (VI), in complete analogy with the above-described case, isomerizes when heated to form the methyl iodide of γ-[benzothiazolyl-(2)]-pyridine (VIII). 3-Ethyl-2-[pyridyl-(γ)]-benzothiazolium iodide likewise isomerizes. 2-[Pyridyl-(γ)]-benzothiazole dissolves in concentrated sulfuric acid with a yellow color which is even weaker than that formed by 2-[pyridyl-(α)]-benzothiazole.

EXPERIMENTAL

I. 2-[Pyridyl-(α)]-benzothiazole

The picolinic acid required for the synthesis was prepared by oxidation of α-picoline [3] and purified through the copper salt. Picolinic acid with m.p. 137° was used. 3.7 g (1 mole) picolinic acid and 3.8 g (1 mole) o-aminothiophenol were well mixed in a thick-walled glass tube which was then sealed and heated for 6 hours with gradual rise of temperature from 140-200° at the rate of 10° per hour. Considerable pressure was released when the tube was opened and the odors of hydrogen sulfide and pyridine were detected; the tube contained colorless cyrstals in a transparent red liquid. The crystals were filtered, washed with a small quantity of alcohol triturated with 10 ml aqueous sodium carbonate, and again filtered and washed with water. An additional crop of product was obtained from the oil by dilution with alcohol and water. There was obtained 2.1 g 2-[pyridyl-(α)]-benzothiazole (33% of the theoretically possible amount). After three crystallizations from alcohol (the solutions were decolorized with carbon) the compound was obtained in the form of colorless needles with m.p. 135°; it contained sulfur and nitrogen.

Found %: N 13.03, 13.22. $C_{12}H_8N_2S$. Calculated %: N 13.21.

2-[Pyridyl-(α)]-benzothiazole was obtained in 60% yield by mixing benzene solutions of o-aminothiophenol and picolinic acid chloride. After purification, the substance prepared by this route had m.p. 135°, and its mixture with the compound prepared as above had the same melting point. This procedure for synthesis of

2-[pyridyl-(α)]-benzothiazole was identical with that described below for 2-[pyridyl-(β)]-benzothiazole from the chloride of nicotinic acid (experiment III).

2[Pyridyl-(α)]-benzothiazole does not dissolve in aqueous solutions of caustic alkalies. It does not dissolve in dilute hydrochloric acid at 20-30°, but it is slightly soluble in the hot acid. It dissolves in concentrated hydrochloric acid in the cold, but addition of excess water to the solution causes it to separate slowly unchanged. Mixing of 5% hot alcoholic solutions of equimolar amounts of picric acid and 2-[pyridyl-(α)]-benzothiazole results in formation of the picrate, which comes down on cooling. M.p. 140-141° after several recrystallizations from alcohol.

Found %: N 15.58, 15.64. $C_{18}H_{11}O_7N_5S$. Calculated %: N 15.87.

With excess of picric acid (3 moles per mole base) a picrate with the same melting point as that of the above compound, and identical with it, was obtained (m.p. of mixed sample 140°).

II. Alkyl halide compounds of 2-[pyridyl-(α)]-benzothiazole

A. Heating of 2-[pyridyl-(α)]-benzothiazole with alkyl halides. 0.2 g 2-[pyridyl-(α)]-benzothiazole and and excess (1 ml) of methyl iodide were heated in a sealed glass tube in boiling water for an hour. The tube was opened, the methyl iodide driven off, and the residue recrystallized from alcohol to give nearly colorless needles with m.p. 134°; the mixture with 2-[pyridyl-(α)]-benzothiazole melted at the same temperature. We got the same result by using ethyl iodide and heating for 5 hours.

B. 3-Methyl-2-[pyridyl-(α)]-benzothiazolium iodide. The preparation was carried out by the method proposed for quaternary salts of benzothiazole by A. I. Kiprianov and Z. N. Pazenko [4]. The starting material, N-methyl-o-aminothiophenol, was prepared likewise by the method of these authors [5]; picolinic acid chloride was prepared by heating the acid with thionyl chloride [6]. Benzene solutions of N-methyl-o-aminothiophenol (4.17 g, 1 mole) and picolinic acid chloride (4.25 g, 1 mole) were gradually mixed; the reaction was exothermic and a yellow viscous precipitate was formed. The mixture was digested for 30 minutes, the liquid was decanted from the solidified precipitate, and the latter was washed with ether and dissolved in 20 ml water with gentle heating. The solution was heated with carbon, filtered and mixed with hot potassium iodide solution (5 g in 5 ml water). The yellow crystalline precipitate was washed with a small amount of water and alcohol (weight of precipitate 4.6 g) and twice recrystallized from alcohol. Yellow crystals were obtained which decomposed violently at 180-182° with formation of a transparent brown liquid, solidifying when cooled.

Found %: I 35.90, 35.85. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

0.6 g 3-methyl-2-[pyridyl-(α)]-benzothiazolium iodide was heated with excess of methyl iodide (1 ml) in a sealed glass tube in boiling water for 5 hours. The methyl iodide was driven off and the residual product, after one crystallization from alcohol, had decomp. temp. 180° and was unchanged starting material.

C. Decomposition of 3-methyl-2-[pyridyl-(α)]-benzothiazolium iodide by heating. 2 g 3-methyl-2-[pyridyl-(α)]-benzothiazolium iodide was heated in a small flask with an exit tube in a sulfuric acid bath. The substance decomposed to form a dark-brown liquid and gave off a vapor. The distillate proved to be methyl iodide (pyridine-methoiodide with m.p. 118-119°). As soon as the whole of the substance taken for the experiment had been converted into liquid, the heating was stopped and the liquid in the flask solidified when cooled. The solid product was twice recrystallized from alcohol and then from petroleum ether to give colorless crystals with m.p. 134°; their mixture with authentic 2-[pyridyl-(α)]-benzothiazole (m.p. 135°) melted at 134°.

Found %: N 12.90, 12.98. $C_{12}H_8N_2S$. Calculated %: N 13.21.

The picrate of the base with m.p. 140° was prepared.

III. 2-[Pyridyl-(β)]-benzothiazole

The nicotinic acid used for the synthesis had m.p. 231°. The starting materials, nicotinic acid and o-aminothiophenol, were taken in equimolecular amounts (10 g each). The condensation was effected as in the case of the analogous reaction with picolinic acid (experiment I), but the sealed tube was heated at 230-235° for 4 hours; on opening, considerable pressure was released and the odors of hydrogen sulfide and pyridine were noticed. To the contents of the tube (colorless crystals in brown oil) was added ether (30 ml); the undissolved crystals were filtered, washed on the filter with ether and then treated twice with 10% aqueous sodium carbonate solution for removal of unreacted nicotinic acid. There was obtained 5.8 g 2-[pyridyl-(β)]-benzothiazole or 34% of the theoretical yield. Crystallization from alcohol (treatment with animal charcoal) gave colorless needles,

m.p. 128-129°, odorless. The compound contains nitrogen and sulfur.

Found %: N 13.07, 13.15; C 68.19; H 3.80; $C_{12}H_8N_2S$. Calculated %: N 13.21; C 67.92; H 3.77.

2-[Pyridyl-(β)]-benzothiazole was prepared in higher yield by condensation of o-aminothiophenol with nicotinic acid chloride. 5.6 g (1 mole) chloride and 5.0 g (1 mole) o-aminothiophenol were dissolved in benzene (10 ml in each case). Into the o-aminothiophenol solution was gradually stirred the solution of the chloride; the reaction was exothermic and a yellow precipitate was formed. The suspension was heated by gentle boiling for 30 minutes, the precipitate was filtered off, washed with benzene, triturated in a mortar with 30 ml 20% aqueous sodium hydroxide, again filtered and washed with water. Yield 4.8 g (57.0% of the theoretical). The substance was identical (mixed melting test) with the above-described 2-[pyridyl-(β)]-benzothiazole.

The picrate of 2-[pyridyl-(β)]-benzothiazole was prepared by mixing hot alcoholic solutions of equimolar amounts of picric acid and the base. The picrate is highly soluble in many organic solvents; it melts at 194-195° (from acetone). Use of excess picric acid gave a picrate identical with the preceding one. 2-[Pyridyl-(β)]-benzothiazole dissolves in 15% hydrochloric acid with evolution of heat; the salt can be isolated by dissolving the base (2 g) in concentrated hydrochloric acid (3 ml), adding alcohol (8 ml), decolorizing the solution with carbon, running in ether (6 ml) and leaving to stand. The salt is recrystallized from a small amount of alcohol. M.p. 215°.

Found %: Cl 14.17, 14.21. $C_{12}H_9N_2ClS$. Calculated %: Cl 14.28.

IV. Alkyl halide compounds of 2-[pyridyl-(β)]-benzothiazole

A. Reaction of 2-[pyridyl-(β)]-benzothiazole with alkyl halides. 0.65 g (1 mole) 2-[pyridyl-(β)]-benzothiazole and 0.43 g (1 mole) methyl iodide were heated for 1 hour in a sealed tube in boiling water. The product of reaction was washed with ether. Yield of methiodide 0.95 g. It was crystallized from alcohol. The mother liquors were heated with carbon to remove resinous impurities. The pure salt melts at 231-232°. An identical product is obtained when using excess of methyl iodide and heating for a longer period.

Found %: I 35.94, 35.75. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The ethiodide of 2-[pyridyl-(β)]-benzothiazole was prepared by the same method. Light-yellow needles with m.p. 223-224° (from alcohol).

Found %: I 34.55, 34.52. $C_{14}H_{13}N_2IS$. Calculated %: I 34.51.

B. 3-Methyl-2-[pyridyl-(β)]-benzothiazolium-iodide. Method of preparation as in experiment II B. 3.8 g (1 mole) nicotinic acid chloride and 3.7 g (1 mole) N-methyl-o-aminothiophenol were reacted. Yield of salt 5.3 g. The product (4.4 g) was dissolved in three times the quantity of hot water and the solution poured into hot water containing KI (2.8 g in 10 ml). The yellow precipitate was filtered, washed with water and recrystallized from 10 times the amount of water. Dense yellow needles were obtained, melting at 206-208° to a liquid which immediately afterwards solidifies and again melts at a higher temperature.

Found %: I 35.97, 35.86. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The starting components did not react when the prepared methiodide (1.2 g) and excess of methyl iodide (3 ml) were heated for 2 hours in a sealed tube in boiling water.

C. Isomerization of 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide. 1 g 3-methyl-2-[pyridyl-(β)]-benzothiazolium iodide was heated in a test tube in a sulfuric acid bath; the thermometer was immersed in the substance. Melting occurs initially at 203° but the liquid immediately solidifies. The temperature of the mass in the test tube was raised to 225°, and the test tube was then cooled. The contents, a light-yellow crystalline mass, weighed 0.96 g. The product of isomerization was recrystallized 3 times from alcohol (decolorization with animal charcoal). The light-yellow, finely crystalline product melted at 232°.

Found %: I 35.93, 36.01. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The mixture of the isomerization product with the methiodide of 2-[pyridyl-(β)]-benzothiazole, prepared by heating the latter with methyl iodide (experiment IV A), melted at 231-232°.

V. 2-[Pyridyl-(γ)]-benzothiazole

Isonicotinic acid was prepared by oxidation of 4-ethylpyridine [7], which was synthesized from pyridine

and acetic anhydride [8]; the isonicotinic acid had m.p. 313° in a sealed capillary. A mixture of equimolar amounts of isonicotinic acid (2.5 g) and o-aminothiophenol (2.5 g) was heated in a sealed glass tube for 4 hours at 210-240°. Slight pressure was released when the tube was opened and hydrogen sulfide was detected. The reaction product was treated with 10 ml 10% aqueous sodium carbonate, and then dissolved in dilute hydrochloric acid (1:1) by heating. The solution was decolorized with carbon and precipitated with 20% sodium hydroxide solution. The crude 2-[pyridyl-(γ)]-benzothiazole was obtained in a yield of 65% of the theoretically possible. Insoluble in water, readily soluble in the cold or when heated in the majority of organic solvents. It was purified by crystallization from a large volume of alcohol and then from petroleum ether. Colorless, crystalline scales, m.p. 136°, odorless.

Found %: N 12.91, 13.10. $C_{12}H_8N_2S$. Calculated %: N 13.21.

The picrate of the base was prepared in nearly quantitative yield by mixing hot alcoholic solutions of the base and picric acid; poorly soluble in hot water, crystallizes from a large volume of acetone with m.p. 237°.

VI Alkyl halide compounds of 2-[pyridyl-(γ)]-benzothiazole

A. Reaction of 2-[pyridyl-(γ)]-benzothiazole with alkyl halides. 0.45 g 2-[pyridyl-(γ)]-benzothiazole and 1 ml methyl iodide were heated in a sealed tube in boiling water for 30 minutes. Acetone was added to the reaction product, and the precipitate was filtered and washed with acetone. The crude product (0.45 g)* was recrystallized from alcohol. The pure methiodide, forming golden, orange-yellow crystals, darkened at 240° and melted at 256°.

Found %: I 35.92, 35.95. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The ethiodide was prepared by heating sealed tubes in boiling water for 1 hour; the same compound was obtained regardless of whether equimolar amounts of reactants were used or whether the ethyl iodide was in excess. It melted at 219-220°; it was crystallized first from alcohol and then from water.

Found %: I 34.40, 34.48. $C_{14}H_{13}N_2IS$. Calculated %: I 34.51.

B. 3-Methyl-2-[pyridyl-(γ)]-benzothiazolium iodide. This quaternary salt was synthesized from N-methyl-o-aminothiophenol and isonicotinic acid chloride by the same procedure as for the analogous salts described in experiments II B and V B. The crude salt-chloride was washed with benzene and ether and converted into the iodide; the latter, after crystallization from water (treatment with animal charcoal), formed yellow crystals which darkened at 195° and melted at 197° to a dark liquid; the latter changed into light crystals with m.p. 253°.

Found %: I 35.98, 36.02. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The starting salt remained unchanged when 3-methyl-2-[pyridyl-(γ)]-benzothiazolium iodide was heated for 5 hours with excess of methyl iodide at 100°.

C. Isomerization of 3-methyl-2-[pyridyl-(γ)]-benzothiazolium iodide. 0.6 g 3-methyl-2-[pyridyl-(γ)]-benzothiazolium iodide was subjected to thermal isomerization as described in experiment IV C. The fusion started at about 160°, and the liquid solidified almost immediately. Heating was stopped as soon as the temperature of the melt had reached 220°. The product of isomerization (weight 0.57 g) was twice recrystallized from alcohol to give golden-yellow (dark) needles with m.p. 256° (after darkening at 240°).

Found %: I 35.84, 35.96. $C_{13}H_{11}N_2IS$. Calculated %: I 35.88.

The mixture of the isomerization product with the methiodide of 2-[pyridyl-(γ)]-benzothiazole, prepared by heating the latter with methyl iodide (experiment VI A), melts at 256°.

SUMMARY

1. The isomeric 2-[pyridyl-(α)]- 2-[pyridyl-(β)]-, and 2-[pyridyl-(γ)]-benzothiazoles were synthesized. The synthesis of these benzothiazole derivatives was effected by condensation of o-aminothiophenol with the pyridinemonocarboxylic acids or their chlorides.

2. The quaternary salts of the 2-pyridylbenzothiazoles were prepared and it was established that: a) after introduction into the 2-position of the benzothiazole molecule of the pyridyl-(α)-, pyridyl-(β)- and pyridyl-(γ)-residues, no basic properties were detected in the benzothiazole; b) the basic properties of pyridine are sharply diminished by the introduction of the benzothiazolyl-(2)-residue in the α-position of its molecule; when the same residue is introduced into the β- or γ-position, the basic properties of the

pyridine are only slightly weakened, although they disappear if a salt is formed at the nitrogen of the benzothiazo residue.

3. Isomerization is observed of the alkyl iodide compounds of 2-[pyridyl-(β)]- and 2-[pyridyl-(γ)]-benzothiazoles in which the alkyl is at the nitrogen atom of the benzothiazole residue; when these quaternary salts are heated to fusion point, the alkyl migrates to the nitrogen atom of the pyridine residue. The methoiodide of 2-[pyridyl-(α)]-benzothiazole decomposes when melted and evolves methyl iodide to leave the corresponding base.

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• See Consultants Bureau translation, p. 1515.
•• See Consultants Bureau translation, p. 29.

REDUCTION OF DIOXINDOLE AT THE DROPPING MERCURY ELECTRODE

I. A. Korshunov and L. N. Sazanova

In a study of the reduction of isatin at the dropping mercury electrode* it was established that isatin belongs to the group of organic substances which undergo reduction at the dropping mercury electrode. Diffusion currents of isatin can be detected when the media are electrolytes with neutral, acid or alkaline reaction. In these solutions isatin is transformed in suitable conditions into isatinic acid with cleavage of the pyrrole ring. The speed of conversion depends on the pH of the solution and on the temperature, and it increases with rising pH and temperature of solution.

The structure of dioxindole is similar to that of isatin, so that we should expect it also to undergo reduction at the dropping mercury electrode with development of diffusion waves. The following experiments confirm the correctness of this assumption.

The dioxindole required for the investigation was synthesized by us by Heller's method: reduction of isatin with zinc dust in glacial acetic acid at room temperature. The dioxindole was extracted with hot alcohol and purified by repeated crystallization. The m.p. of the synthesized product was 178-180°. The investigation was carried out with an alcoholic solution of dioxindole containing 80% ethyl alcohol. Prior to the polarographic measurements the starting solution was mixed with the required solution of the medium in the proportion which gave the required concentration. Buffered and nonbuffered solutions were used as solutions of indifferent electrolytes. Buffered solutions were prepared from solutions of boric, acetic and phosphoric acids, neutralized with sodium hydroxide solution.

The unbuffered solutions were 1 N solution of lithium chloride, 2 N solution of lithium nitrate, a mixture of 0.5 N ammonia solution and ammonium chloride, and 0.2 N potassium hydroxide solution.

The electrolytic cell and the dropping mercury electrode were of normal design. Measurements were performed with a capillary which delivered mercury at the rate of 1.38 mg/sec and the period of dropping was 3.8 sec. The evolved oxygen was not removed since dissolved oxygen did not interfere with the polarographic measurements of the fairly concentrated dioxindole solutions. All measurements were performed at a temperature of 20 $\pm$0.5° in a thermostat. The half-wave potential of dioxindole was measured in relation to the reference saturated calomel electrode whose potential was arbitrarily assumed to be zero.

Diffusion currents were measured with the help of a visual polarograph and a galvanometer with a sensitivity of $0.49 \cdot 10^{-9}$ A per scale division.

EXPERIMENTAL RESULTS AND THEIR EVALUATION

Dioxindole diffusion currents with horizontal portions at the start and finish of the polarization curve were observed in buffer solutions whose pH was less than 5.15 5.20. In buffer solutions whose pH was higher than 5.15-5.20, a precipitate came down and diffusion waves of the reduction are not formed (Figure 1). In Table 1 are presented results of measurements of the half-wave potentials of dioxindole and values of the diffusion currents of the latter when using buffered solutions of the composition indicated above as indifferent electrolytes.

It follows from the data of Table 1 that the half-wave potential of dioxindole in buffered solutions remains substantially constant with changing pH of the medium and changing concentration of the substance which is being reduced.

The reduction of dioxindole in presence of solutions of lithium chloride and nitrate, ammonia and caustic alkalies is accompanied by formation of one diffusion wave on the polarograms. The numerical values of the potentials and diffusion currents of dioxindole in a medium of unbuffered solutions are set out in Table 2.

A yellow precipitate is formed in potassium hydroxide solutions and the diffusion current of dioxindole could not be detected.

* I. A. Korshunov and M. K. Shchennikova, J. Phys. Chem. USSR, 24, 813 (1950).

TABLE 1

Half-Wave Potential and Diffusion Currents of Dioxindole in Buffer Solutions

pH value	$\pi^{1/2}$ (in V)		i_d (in μA)	
	Conc. of dioxindole (in mmol/l)		Conc. of dioxindole (in mmol/l)	
	1.9	3.5	1.9	3.5
1.03	1.06	1.06	4.35	8.84
2.50	1.05	1.05	4.54	8.80
3.25	1.04	1.06	4.56	8.80
3.76	1.06	1.04	4.54	8.43
4.17	1.07	1.07	4.47	8.43
4.76	1.06	1.04	4.54	8.23
5.15	1.06	1.04	4.54	8.43

TABLE 2

Half-Wave Potentials and Diffusion Currents of Dioxindole in a Medium of Unbuffered Solutions. Concentration of Dioxindole 1.9 mmol/l

Comp. of medium	$\pi^{1/2}$ (in V)	i_d (in μA)
1 N lithium chloride	1.06	3.92
1 N lithium nitrate	1.02	3.92
0.5 N ammonium chloride and 0.5 N ammonia	1.32	4.92
0.2 N potassium hydroxide	No wave	No wave

In the reduction of dioxindole at the dropping mercury electrode in an acid medium, a direct proportionality was observed between the diffusion current and the concentration; the following relation was valid between the current (in microamperes) and the dioxindole content (in millimoles per liter) for our capillary:

$$i_d = 2.46\ C,$$

where i_d is the diffusion current and C is the dioxindole concentration.

The straight-line plot for dioxindole in presence of a buffered solution of pH = 2.5 is given in Figure 2.

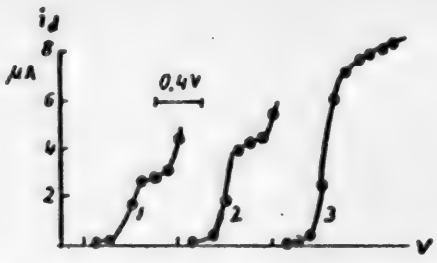

Fig. 1. Diffusion currents of dioxindole solutions in a medium of a buffer solution with pH = 2.5. 1) Concentration 1.1 mmol/l 2) concentration 1.9 mmol/l; 3) concentration 3.8 mmol/l.

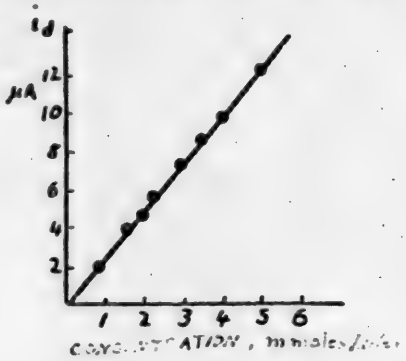

Fig. 2. Straight-line plot for dioxindole in a buffered solution with pH = 2.5.

The Ilkovic equation may be utilized for determination of the number of electrons participating in the reduction reaction:

$$i_d = 605\ nD^{1/2}n^{2/3}\ t^{1/6}C.$$

The diffusion coefficient of dioxindole, D, enters into this equation. We arbitrarily assumed the latter to be $0.3 \cdot 10^{-5}$ $cm^2 sec^{-1}$, no literature data being available.

On substituting our data and the above magnitude of the diffusion coefficient we obtain a value close to 2 for n, which indicates the two-electrode process of the reduction.

The Heyrovsky-Ilkovic equation for the polarographic wave can also be applied to the determination of the number of electrons participating in the reduction reaction of the dioxindole molecule:

$$\pi = \pi_{1/2} + \frac{2.3RT}{nF} \log \frac{i_d - i}{i}.$$

This equation is in good agreement with the experimental data for the dependence of the diffusion current on the potential of the dropping mercury electrode. All the experimental points lie on a straight line; however, the slope of the straight line in the φ versus log $\frac{i_d - i}{i}$ plot gives value less than unity for n. The fractional value of n is probably due to the irreversibility of the process of reduction and the complexity of the reaction at the electrode.

SUMMARY

1. It is shown that the dioxindole molecule is reduced at the dropping mercury electrode in media with an acidic reaction.

2. The number of electrons participating in the reduction reaction of the dioxindole molecule is found.

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ISOQUINOLINE COMPOUNDS

VII. SYNTHESIS OF β-(α'-DIETHYLACETAL)-PROPYLGLUTARIC ACID

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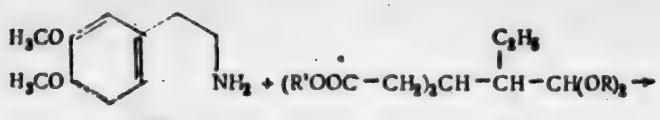
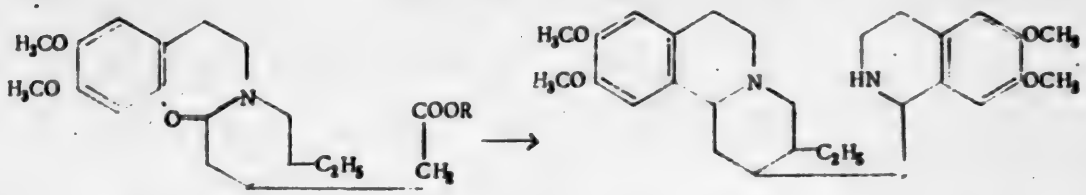
We have already drawn attention [1] to the importance in work on the synthesis of the alkaloid, emetine, of the investigation of compounds with a carbon skeleton corresponding to the central portion of the molecule of the alkaloid. The following compounds were previously prepared for this purpose: a) Ethyl ester of β-(α'-cyano)-propylglutaric acid; b) γ-ethyl-δ-valerolactone-β-acetic acid; and c) ethyl ester of β-(α'-bromometho)-propylglutaric acid [2]. In addition we have now developed a method for preparation of β-(α'-diethylacetal)-propylglutaric acid (I). By condensing this acetal with homoveratrylamine (II) we synthesized the ester of N-homoveratryl-δ-ethyl-α-piperidone-γ-acetic acid (III), which we previously described [2] and which leads to emetine (IV) through a series of steps:

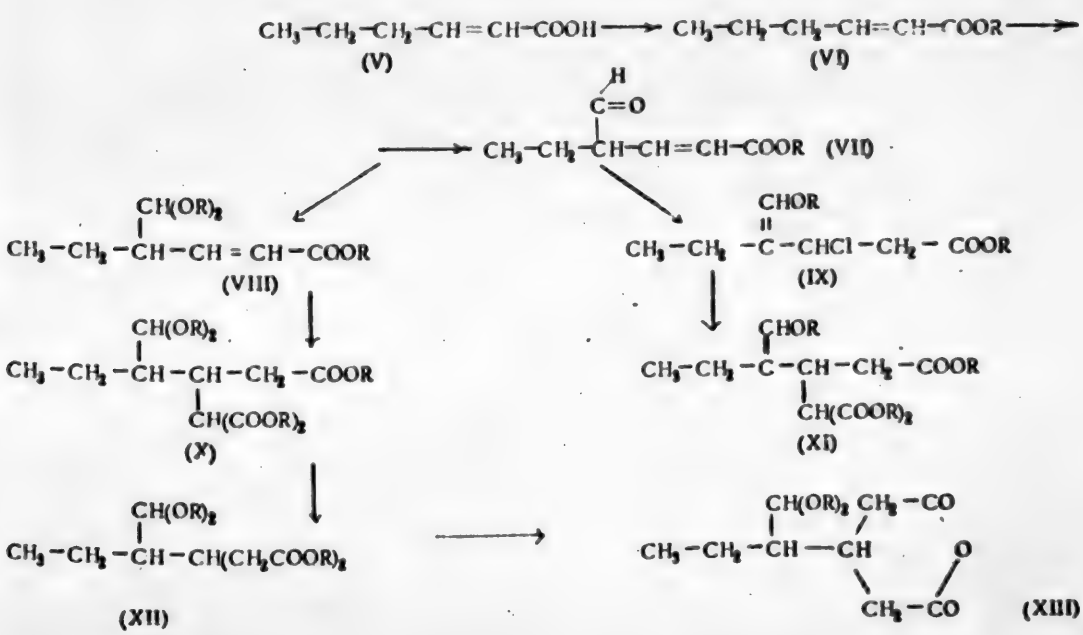


(II) (I)



(III) (IV)

We effected the synthesis of β-(α'-diethylacetal)-propylglutaric acid (I, R' = H) by the following scheme.



(V) (VI) (VII) (VIII) (IX) (X) (XI) (XII) (XIII)

*Deceased

β-Propylacrylic acid (V), prepared from butyraldehyde and malonic acid [3], is esterified to (VI) which is then condensed with ethyl formate to give the formyl derivative of the ester of β-propylacrylic acid [4] (VII). Heating of the ester of γ-formyl-α,β-hexenoic acid (VII) with ethyl orthoformate in a medium of alcohol in presence of a small amount of ammonium chloride as catalyst gives the ester of the acetal of γ-formyl-α,β-hexenoic acid [5] (VIII). On the other hand, reaction of the ester (VII) with alcohol in a current of dry hydrogen chloride gives the partial acetal, and a molecule of hydrogen chloride adds on at the double bond [6] (IX).

Great difficulties are encountered in working with both the formyl derivatives and the acetals of the ester of hexenoic acid. Like other acrylic acid derivatives, these compounds rapidly polymerize. The pure compounds could be isolated by distilling them in a current of inert gas and in presence of a small amount of hexamethylene tetramine as stabilizer. Condensation of the ester of both of the acetals of γ-formyl-α,β-hexenoic acid (VIII and IX) with ethyl malonate in presence of sodium alcoholate leads to the corresponding tricarboxylic esters (X and XI). Saponification of the ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid (X) with the calculated amount of an aqueous alcoholic solution of potassium hydroxide followed by acidification and decarboxylation results in separation of β-(α'-diethylacetal)-propylglutaric acid (XII), distillation of which in vacuum leads to the anhydride of the acid (XIII).

EXPERIMENTAL

β-Propylacrylic acid (V) is prepared by the usual method, e.g., by heating a stirred mixture of 60 g (1 mole) freshly distilled butyraldehyde (b.p. 75°), 87 g (1 mole) malonic acid, 40 ml pyridine and a few drops piperidine for 3 hours at 60-70° and for the same period at 110°. The pyridine is removed and the residue distilled in vacuum.

β-Propylacrylic acid is a white crystalline substance, highly soluble in alcohol and ethers, poorly soluble in cold water. B.p. 98-102° at 8 mm[2]; m.p. 34-35°. Yield 75 g, or 79% of the theoretical.

Ethyl ester of β-propylacrylic acid (VI) is prepared by heating 85 g (1 mole) β-propylacrylic acid, 120 ml absolute ethyl alcohol and 12 ml sulfuric acid(sp.g. 1.84) for 7 hours. B.p. 174-175° [2]. Yield 81 g or 76% of the theoretical. Colorless liquid, soluble in benzene, ether, alcohol and chloroform, insoluble in water.

Ethyl ester of γ-formyl-α,β-hexenoic acid (VII). Into 13 g (1 g-atom) metallic sodium in 400 g absolute toluene is run 50 g (1.2 moles) freshly distilled ethyl formate and 80 g (1 mole) ethyl β-propylacrylate. Bubbles of hydrogen are evolved. The mass acquires an orange color and gradually deposits a precipitate of the sodium compound of the ethyl ester of γ-formyl-α,β-hexenoic acid. The reaction usually extends over a period of 24 hours. The reaction mixture is carefully poured onto ice. The toluene layer is separated and the aqueous layer is extracted 3-4 times with benzene for removal of unreacted ethyl ester of propylacrylic acid. The aqueous solution is cooled and acidified with phosphoric acid (Congo red test). The formyl derivative is extracted with ether, and the extract is dried with sodium sulfate. Distillation of the solvent leaves 52 g (54%) of technical ester of γ-formyl-α,β-hexenoic acid. From 10 g of the substance distilled at 65-70° (1 mm) in a nitrogen stream in presence of a small amount of hexamethylenetetramine was obtained 2.9 g ethyl ester of γ-formyl-α,β-hexenoic acid. Colorless liquid, soluble in benzene, alcohol and ether. It gives a violet coloration with an aqueous solution of iron chloride[3].

d_{20}^{20} 1.0412, n_D^{20} 1.4648. MR_D 45.17. Calculated MR_D 44.96 (for the aldehyde form), 46.01 (for the enol form).

3.005 mg substance: 7.020 mg CO_2; 2.320 ml H_2O. 2.995 mg substance: 7.010 mg CO_2; 2.360 mg H_2O. Found %: C 63.70, 63.82; H 8.63, 8.81. $C_9H_{14}O_3$. Calculated %: 63.48, H 8.29.

Owing to the fact that a large proportion of the ethyl ester of γ-formyl-α,β-hexenoic acid polymerizes during distillation, the next stage – the preparation of the acetal – was performed both with the distilled and the technical material, but there was little difference in yield.

Ethyl β-chloro-γ-ethoxymethylenecaproate (IX). A mixture of 11 g (1 mole) sodium compound of the ethyl ester of γ-formyl-α,β-hexenoic acid, 12 g (4.55 moles) absolute ethyl alcohol and 45 ml absolute ether, previously saturated with 4.6 g (2.2 moles) hydrogen chloride are mixed with external cooling for 2 hours and then at room temperature for 14 hours. The reaction mixture is treated with sodium bicarbonate for complete neutralization of the hydrogen chloride. The resultant precipitate is filtered and washed 3 times with 15 ml lots of ether. The solvent is driven off and the residue distilled. b.p. 68-78° at 5 mm, yield 4.1 g (30.5% of the theoretical). A colorless liquid with an unpleasant odor, soluble in alcohol, benzene, ether and chloroform.

d_{20}^{20} 0.9927; n_D^{20} 1.4459; MR_D 62.98, calculated 60.70.

2.935 mg substance: 5.980 mg CO_2; 2.040 mg H_2O. Found %: C 55.56; H 7.77. $C_{11}H_{19}O_3Cl$. Calculated %: 56.25, H 8.16.

Ethyl ester of γ-(α'-diethylacetal)-α,β-hexenoic acid (VIII). To a mixture of 5 g (1 mole) distilled ethyl ester of γ-formyl-α,β-hexenoic acid and 4.35 g (1 mole) freshly distilled ethyl orthoformate is added 0.1 g (0.63 mole) ammonium chloride in 2 ml absolute alcohol. The mixture is then heated on a boiling water bath for 30 minutes. On the following day the liquid is decanted off, mixed with double the quantity of ether and washed several times with 5% ammonia solution until the turbidity disappears, and then with water until neutral. The ethereal solution is dried with potassium carbonate. The residue after removal of the solvent is distilled in vacuum in a nitrogen stream in presence of hexamethylenetetramine; b.p. 79-83° at 0.8 mm. Yield 2.55 g, or 35.6% of the theoretical. The ester is a colorless liquid, soluble in alcohol, ether and chloroform; insoluble in water.

3.135 mg substance: 7.325 mg CO_2; 2.650 mg H_2O. Found %: C 63.71; H 9.46. $C_{21}H_{34}O_4$. Calculated %: C 63.88; H 9.90.

Ethyl α-carbethoxy-β-(α'-ethoxymethylene)-propylglutarate (XI). To sodium alcoholate prepared from 4 ml absolute alcohol and 0.22 g (1 mole) metallic sodium is added at 30-40° 3 g (2 moles) ethyl malonate and the mixture kept at this temperature for 30 minutes. Addition is then made of 2 g (1 mole) ethyl ester of β-chloro-γ-ethoxymethylenecaproic acid. The mixture is heated for 5 hours. On the following day the alcohol is distilled off and the residue poured on to ice. The separated oil is extracted with benzene and the extract is dried with calcined sodium sulfate. The residue after removal of the benzene is distilled with addition of hexamethylenetetramine; b.p. 148-149° at 2.5 mm. Yield 1.7 g or 55.7 % of the theoretical. The ester is a colorless liquid, soluble in alcohol and ether, insoluble in water.

3.260 mg substance: 7.190 mg CO_2; 2.510 mg H_2O. 2.920 mg substance: 6.470 mg CO_2; 2.290 mg H_2O. Found %: C 60.14, 60.42; H 8.61, 8.77. $C_{18}H_{32}O_7$. Calculated %: C 60.29; H 8.44.

Ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid (X). To sodium alcoholate prepared from 0.6 g(1 g-atom) sodium and 10 ml absolute alcohol is added 7.8 g (2 moles) ethyl malonate and 6 g (1 mole) ethyl ester of γ-(2'-diethylacetal)-α,β-hexenoic acid. The mixture is heated on a boiling water bath for 5 hours. The ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid is separated by the usual method. B.p. 150-163° (1 mm). Yield 4.8 g or 48.3% of the theoretical. Colorless liquid, soluble in ether, alcohol and benzene, insoluble in water.

3.175 mg substance: 6.910 mg CO_2; 2.485 mg H_2O. 3.055 mg substance: 6.655 mg CO_2; 2400 mg H_2O. Found %: C 59.34, 59.40; H 8.75, 8.79. $C_{20}H_{38}O_8$. Calculated %: C 59.36; H 8.97.

β-(α'-Diethylacetal)-propylglutaric anhydride (XIII). To 5.5 g (1 mole) ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid is added a solution of 4.6 g (6 moles) potassium hydroxide in 45 ml water and 45 ml methyl alcohol, and the mixture is refluxed for 5 hours. After distilling off the alcohol, the aqueous solution (cooled to 0°) of the potassium salt of the ethyl ester of α-carbethoxy-β-(α'-diethylacetal)-propylglutaric acid is mixed with 150 ml ether and carefully treated with hydrochloric acid until weakly acid. The ether layer is separated. Free acid is extracted from the aqueous solution with ether. After distilling off the solvent, the residue is heated on an oil bath for an hour at 160° (20 mm), after which it is distilled: b.p. 155-157° (4mm). Yield 1.3 g or 37% of the theoretical. The anhydride is a viscous liquid, darkening in the air, soluble in benzene, ether and alcohol; slightly soluble in water.

3.005 mg substance: 6.695 mg CO_2; 2.295 mg H_2O. 2.980 mg substance: 6.655 mg CO_2; 2.265 mg H_2O. Found %: C 60.75, 60.90; H 8.54, 8.50. $C_{13}H_{22}O_5$. Calculated %: C 60.43; H 8.59.

SUMMARY

1. Syntheses were effected of β-(α'-diethylacetal)-propylglutaric acid and its anhydride, intermediates for the synthesis of emetine.

2. Methods were developed for the preparation of the ethyl ester of γ-formyl-α,β-hexenoic acid and the ethyl-ester of γ-(α'-diethylacetal)-α,β-hexenoic acid, as well as of substances confirming their structure: the ethyl ester of β-chloro-γ-ethoxymethylenecaproic acid and the ethyl ester of α-carbethoxy-β-(α'-ethoxymethylene)-propylglutaric acid.

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* See Consultants Bureau translation, p. 1931.

ISOQUINOLINE COMPOUNDS

VIII. CONDENSATION OF α'-SUBSTITUTED β-PROPYLGLUTARIC ACIDS WITH HOMOVERATRYLAMINE

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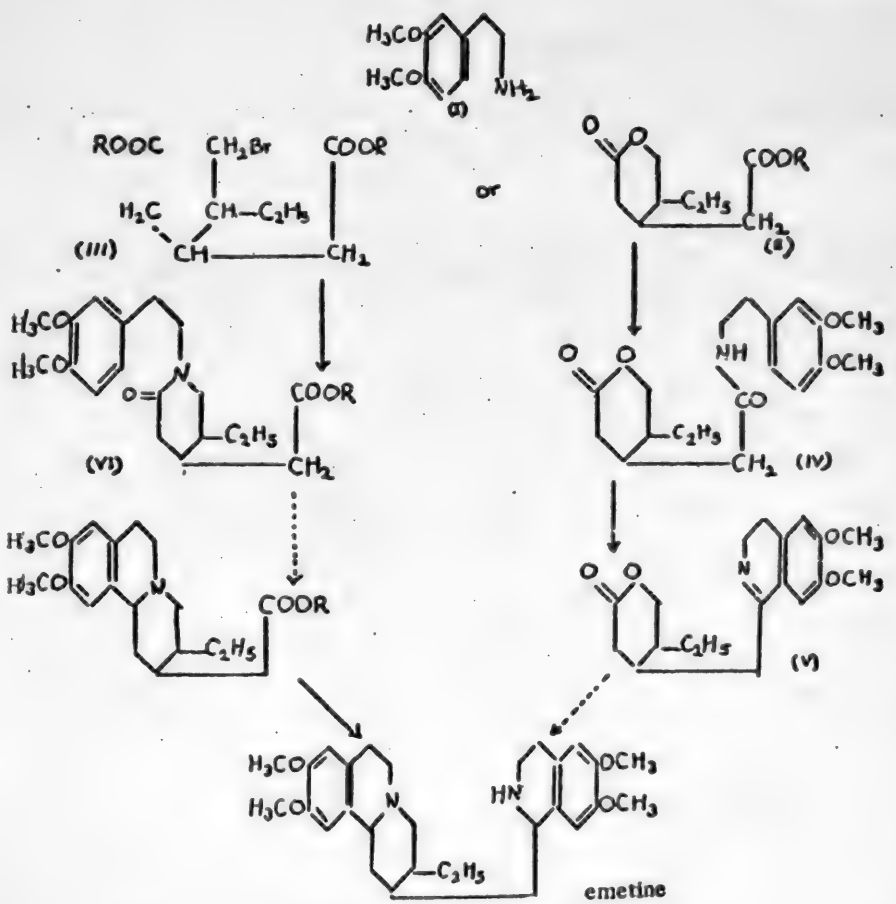
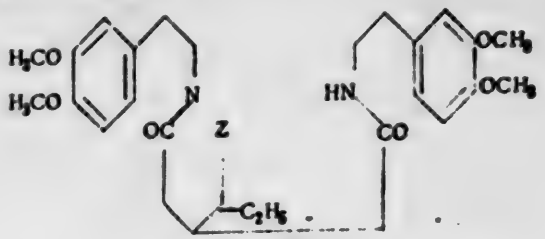
The basis of our synthesis of the alkaloid emetine [1] is the condensation of esters of α'-substituted β-propylglutaric acids with homoveratrylamine. We had earlier described the reaction between homoveratrylamine and the ester of β-(α'-cyano)-propylglutaric acid which successfully led through a series of intermediate compounds to the preparation of emetine.

In this paper we describe the condensation of homoveratrylamine (I) with γ-ethyl-δ-valerolactone-γ-acetic acid (II) and β-(α'-bromometho)-propylglutaric acid (III), previously prepared by another route [2].

These syntheses are characterized by the following general scheme:



Reaction of starting compounds (II) and (III) with one molecule of homoveratrylamine (I) gives, respectively, the homoveratrylamide of γ-ethyl-δ-valerolactone-β-acetic acid (IV) [which is transformed with phosphorous oxychloride into the 6,7-dimethoxy derivative of dihydroisoquinoline (V)] and the ester of N-homoveratryl-δ-ethyl-α-piperidon-γ-acetic acid (VI). By performing this reaction with excess of homoveratrylamine we can isolate the diamides of structure (VII).



(VII)

the dihomoveratrylamide of β-(α'-oxymetho)-propylglutaric acid (when Z = CH_2OH) and the dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid (when Z = CH_2Br).

As we have previously shown [1], compounds (IV to VII) are intermediates for the synthesis of emetine. For example, cyclization of compounds (VII) followed by reduction leads to emetine; moreover, compounds (V) and (VI) can be utilized for elucidation of the stereochemical structure and of the effect of individual elements in the molecule on the physiological action of this alkaloid.

EXPERIMENTAL

1. γ-Ethyl-δ-valerolactone-β-acetyl chloride. 4.5 g γ-ethyl-δ-valerolactone-γ-acetic acid is dissolved in 5 ml thionyl chloride and the solution left at room temperature for 2 hours. The excess of thionyl chloride is distilled off and the residue is distilled in vacuum. B.p. of the chloride 137-138° at 3 mm. Yield 3.7 g or 47% of the theoretical.

2. Homoveratrylamide of γ-ethyl-δ-valerolactone-β-acetic acid (IV). 3.4 g homoveratrylamine and 1.7 g dry pyridine are dissolved in 50 ml benzene. Into the benzene solution is stirred a solution of 3.7 g γ-ethyl-δ-valerolactone-β-acetyl chloride in 10 ml benzene. Pyridine hydrochloride is precipitated almost at once. Stirring is then continued for an hour at room temperature, after which water is added to dissolve the pyridine hydrochloride, the benzene solution is separated from the aqueous layer and washed in succession with dilute hydrochloric acid and sodium bicarbonate solution. After drying with sodium sulfate, the benzene is distilled off in vacuum. The residue is a light-brown, viscous oil; yield 5.6 g or 88% of the theoretical.

10.760 mg substance: 0.367 ml N_2 (23°, 728 mm). Found %: N 3.77. $C_{19}H_{27}O_5N$. Calculated %: N 3.92.

3. γ-Ethyl-δ-valerolactone-β-(1-methylene-6,7-dimethoxy-3,4-dihydroisoquinoline) (V). A solution of 5 g homoveratrylamide of γ-ethyl-δ-valerolactone-β-acetic acid and 7.5 ml phosphorus oxychloride in 50 ml dry toluene is heated at a gentle boil for an hour. After cooling to room temperature the faintly colored toluene solution is decanted from the viscous precipitate. The latter is twice washed with ether and 30 ml water acidified with 2 ml hydrochloric acid is added. The acid solution is freed from insoluble resins and treated with saturated sodium iodide solution until precipitation is complete. The resultant oil is extracted with chloroform. After drying, the chloroform is driven off in vacuum, and the residue is dissolved in ether and recovered as a light yellow amorphous powder. Recrystallization from alcohol gives the finely crystalline yellowish hydroiodide of γ-ethyl-δ-valerolactone-β-(1-methylene-6,7-dimethoxy-3,4-dihydroisoquinoline). M.p. 199-201°. Yield 2.1 g or 32% of the theoretical:

4.475 mg substance: 0.127 ml N_2 (22°, 756 mm). Found %: N 3.27. $C_{19}H_{21}O_4N \cdot HI$. Calculated %: N 3.05.

M.p. of the picrate, recrystallized from alcohol, 181-182°.

3.750 mg substance: 0.324 ml N_2 (22°, 756 mm). Found %: N 9.94. $C_{25}H_{25}O_{11}N_4$. Calculated %: N 9.98.

4. Diethyl ester of β-(α'-bromometho)-propylglutaric acid (III). A solution of 6 g γ-ethyl-δ-valerolactone-β-acetic acid in 50 ml absolute alcohol is saturated with dry hydrogen bromide at 0° and allowed to stand for 12 hours. The alcohol is distilled off in vacuum and the residue poured into cold water and extracted with benzene. The benzene solution is washed with a sodium bicarbonate solution. The benzene is taken off in vacuum and the

ester is distilled at 140-141° (3 mm). Yield 7.5 g or 72% of the theoretical; n_D^{20} 1.4628.

3.020 mg substance: 5.325 mg CO_2; 1.945 mg H_2O. Found %: C 48.12; H 7.21 $C_{13}H_{23}O_4Br$. Calculated %: C 48.28; H 7.17.

5. Ethyl ester of N-homoveratryl- δ-ethyl- α-piperidon- γ-acetic acid (VI). A solution of 5 g diethyl ester of β-(α'-bromometho)-propylglutaric acid and 12 g homoveratrylamine in 30 ml dry toluene is heated on an oil bath at a gentle boil for 2½ hours. After cooling, crystals of the hydrobromide are precipitated. Water is added and the toluene solution is separated from the aqueous layer and washed with dilute hydrochloric acid. The toluene is taken off in vacuum and the residue distilled. B. p. 227-231° (2 mm). Yield 1.3 g (21.6% of the theoretical).

3.105 mg substance: 7.645 mg CO_2; 2.195 mg H_2O. 3.010 mg substance: 7.410 mg CO_2; 2.250 mg H_2O. 5.169 mg substance: 0.171 ml N_2 (23°, 763 mm). Found %: C 67.19, 67.18; H 7.91, 8.36; N 3.83. $C_{21}H_{31}O_7N$. Calculated %: C 66.80; H 8.27; N 3.71.

6. Dihomoveratrylamide of β-(α-oxymetho)-propylglutaric acid (VII, Z = CH_2OH). 3 g γ-ethyl- δ-valerolactone-β-acetic acid (III) is heated with 8 g homoveratrylamine for 4 hours at 190-200°. Water separates. After cooling, the light-brown mass is dissolved in benzene. The benzene solution is washed in succession with dilute hydrochloric acid and sodium carbonate solution. After drying with sodium sulfate, the benzene is taken off in vacuum; the residue weighs 5.8 g (68% of the theoretical). The product is a nonmobile oil, insoluble in ether.

3.280 mg substance: 7.845 mg CO_2; 2.365 mg H_2O. Found %: C 65.27; H 8.07. $C_{39}H_{62}O_7N_2$. Calculated %: C 65.61; H 7.98

7. Chloride of β-(α'-bromometho)-propylglutaric acid. 4 g β-(α'-bromometho)-propylglutaric acid is heated with 5 ml thionyl chloride on a water bath at 50° for 2 hours and then at the boiling point of the thionyl chloride for an hour. The excess of thionyl chloride is distilled off and the residue distilled in vacuum. B.p. of the acid chloride 141-143° (2 mm). Yield 3.5 g (77.5% of the theoretical).

8. Dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid (VII, Z = CH_2Br). To a benzene solution of 7.3 g homoveratrylamine, cooled with iced water, is added gradually, with stirring, a benzene solution of 5 g β-(α'-bromometho)-propylglutaric acid chloride. Homoveratrylamine hydrochloride begins to separate almost immediately. After the addition of the acid chloride, the mixture is stirred for 1½ hours at room temperature. Water is then added to dissolve the homoveratrylamine hydrochloride, and the benzene solution is washed in succession with dilute hydrochloric acid (1:2) and sodium carbonate solution. After drying with sodium sulfate, the benzene is distilled off in vacuum. The residue weighs 4.9 g (83% of the theoretical). For the purpose of analysis the dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid was reprecipitated from alcohol by addition of ether. A light orange, viscous, nonmobile oil.

4.845 mg substance: 0.214 ml N_2 (22°, 740 mm). Found %: N 4.98. $C_{39}H_{61}O_6N_2Br$. Calculated %: N 4.72.

SUMMARY

Condensation of homoveratrylamine with γ-ethyl- δ-valerolactone-β-acetic acid or β-(α'-bromometho)-propylglutaric acid gave: γ-ethyl- δ-valerolactone-β-(1-methylene-6,7-dimethoxy-3,4-dihydroisoquinoline), the ester of N-homoveratryl- δ-ethyl-α-piperidon- γ-acetic acid, the dihomoveratrylamide of β-(α'-bromometho)-propylglutaric acid, and the dihomoveratrylamide of β-(α'-oxymetho)-propylglutaric acid – principal intermediate products in the synthesis of emetine.

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* See Consultants Bureau translation, p. 1931.

THE ALKALOIDS OF OROBANCHE LUTEA

I. A NEW ALKALOID, OROBANCHAMINE

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The plant Orobanche lutea belongs to the Orobanchaceae family. It is a chlorophyll-free parasite which parasitizes the roots of plants. The material used in the present investigation was collected in the Transcaucasus. The pulverized above-ground parts of the plant were treated with ammonia solution and extracted with dichloroethane to yield a weak base in the pure, crystalline form. This product did not give an alkaline reaction to phenolphthalein. The alkaloid melts at 193-194° and has $[\alpha]_D$ +33.92°. The results of the elementary analyses given in the experimental part correspond most closely to the formula $C_{28}H_{31}O_{14}N$, but this formula cannot be considered final. With such a large molecular weight a change in formula by two hydrogen atoms only changes the content of the latter by 0.37%, which is almost at the limit of analytical accuracy. Judging by the constants, but mainly by the empirical formula, the isolated alkaloid is a new, previously undescribed substance and we therefore propose the name of orobanchamine. The content of the alkaloid in the plant is very small: in the specimens that we investigated it did not exceed 0.06%, calculated on the air-dry material. The oxygen content is unusually high for an alkaloid and suggests the possibility of orobanchamine being a glucoalkaloid. Determination of the active hydrogen content by the Tserevitinov method, however, compels this supposition to be rejected.

EXPERIMENTAL

1.8 kg pulverized, air-dry above-ground parts of the plant were treated with 10% ammonia solution until a strong odor of ammonia persisted, and exhaustively extracted with dichloroethane. The dichloroethane extract was exhaustively extracted with 5% sulfuric acid solution. The acid solution was purified by shaking with ether, the ether was separated, and the acid solution was treated with excess of strong ammonia solution before being extracted with chloroform. The chloroform extract was dried with sodium sulfate, filtered, and the chloroform removed by distillation first at the ordinary pressure and toward the end in vacuum. There remained an oil which crystallized fairly quickly on standing. The crystalline mass was purified from the accompanying resins by trituration with 5 ml of a mixture of 2 parts chloroform and 1 part petroleum ether (b.p. 60-80°). After filtration and drying, the product weighed 1.1 g. It was recrystallized from 20 times the amount of the same mixture of chloroform and petroleum ether. After two recrystallizations it formed fine, colorless prisms melting at 193-194° and maintaining the same melting point after further recrystallizations.

0.0339 g subst.: 1 ml alcohol; 1 1 dm; α_D +1.15°, $[\alpha]_D$ +33.92°. 4.567 mg subst.: 7.973 mg CO_2; 2.462 mg H_2O. 4.134 mg substance: 7.2[illegible] mg CO_2; 2.2[illegible] mg H_2O; 8.970 mg substance: 0.221 ml N_2 (23°, 736 mm). 7.210 mg substance: 0.183 ml N_2 (23°, 735 mm). Found %: C 47.61, 47.58; H 6.03, 6.13; N 2.75, 2.83. $C_{28}H_{31}O_{14}N$. Calculated %: C 47.13; H 6.13; N 2.75.

Sulfur and active hydrogen were not found.

Orobanchamine is readily soluble in alcohol, not so soluble in chloroform and ether, poorly soluble in water and petroleum ether.

SUMMARY

A new alkaloid of the composition $C_{28}H_{31}O_{14}N$, named orobanchamine, has been isolated from Orobanche lutea, a parasitic plant, and characterized.

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• Deceased.

INVESTIGATION OF THE ALKALOIDS OF STIZOLOPHUS BALSAMITA (LAM.)

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Stizolophus balsamita (Lam.) (A. Takht. = Centaurea balsamita Lam.) is an annual plant of the Compositae family. The above-ground portion consists of thin, rod-like branched stalks up to 80 cm in length. The leaves are lanceolate. The racemes are large, oviform panicles with yellow flowers. The plant is common in Transcaucasus, and in the Gruzian, Azerbaijan and Armenian SSR. The local population uses aqueous decoctions of stizolophus, as a medicament, internally for fevers, externally as a gargle in tonsilitis and as a fomentation in shingles.

The material for study of the alkaloids and their pharmaceutical and anti-bacterial properties was gathered in 1948 during the phenophase of budding on June 27-28 on the dry slopes by the River Kura above the village of Aspindza and on July 19 during the climax of flowering in the plain to the east of the town of Tbilis where the plant is found in enormous quantities.

Extraction with dichloroethane of the ammonia-treated above-ground parts of the plant enabled us to isolate a crystalline, optically active ($[\alpha]_D$ + 24.6°) base which melted at 122-123° with decomposition. The analytical results point to the formula $C_{15}H_{23}NO_5$. Judging by the empirical formula and the constants, the base is a new compound, not previously described in the literature. We propose the name "stizolophine" for it.

The content of the alkaloid in the specimens of Stizolophus balsamita that we examined is about 0.3%*. The substance is readily soluble in alcohol and acetone, less soluble in water and chloroform. Aqueous solutions of the base (1 g in 100 g water) have a pH of 8.8. Solutions in dilute (5-10%) inorganic acids are unstable; on standing or on short-period heating, they develop a cherry-red color; we were unable to recover the unchanged base from these solutions. The majority of the salts of stizolophine that we prepared were amorphous; the only ones that crystallized were the salicylate $C_{15}H_{23}NO_5 \cdot C_7H_6O_3$, melting at 187-188°, and the viridiflorate** $C_{15}H_{23}NO_5 \cdot C_7H_{14}O_4$, m.p. 168-169°.

A biological study of stizolophine, carried out in the pharmacological department of the All-Union Research Institute of Pharmaceutical Chemistry by M. D. Mashkovsky and S. N. Milovanovaya, showed that the alkaloid possesses little activity pharmacologically and in respect of antibacterial action.

EXPERIMENTAL

4.6 kg air-dry, pulverized, above-ground parts of the plant were wetted with 10% ammonia solution and exhaustively extracted with dichloroethane. The dichloroethane extracts were shaken with 10% sulfuric acid solution used without excess in quantity sufficient for neutralization. The acid solution was treated, while cooling, with excess of 25% ammonia solution and extracted with chloroform. The chloroform extracts were dried with sodium sulfate before evaporation to a small volume. On cooling, stizolophine crystallized in the form of white needles which filled the whole of the liquid. Two crystallizations from chloroform gave 12 g white, very slender crystals, m.p. 122-123°.

3.470 mg substance: 7.728 mg CO_2; 2.482 mg H_2O. 3.871 mg substance: 8.648 mg CO_2; 2.724 mg H_2O. 3.173 mg substance: 6.997 mg CO_2; 2.201 mg H_2O. 4.985 mg substance: 10.990 mg CO_2; 3.401 mg H_2O. 7.920 mg substance: 0.327 ml N_2 (23.5°, 725 mm). 9.360 mg substance: 0.378 ml N_2 (23.0°, 734 mm). 6.130 mg substance: 0.255 ml N_2 (24.5°, 734 nm). 6.700 mg substance: 0.269 ml N_2 (22.5°, 733.5 mm) 4.864 mg substance: 5.47 ml $Na_2S_2O_3$. 0.0756 g substance: 41.31 g benzene: Δt 0.033°. Found %: C 60.74, 60.93, 60.14, 60.12; H 8.00, 7.87, 7.76, 7.63; N 4.55, 4.52, 4.60, 4.47; NCH_3 10.86; M 281. $C_{14}H_{20}O_5$ (NCH_3). Calculated %: C 60.59; H 7.80; N 4.71; NCH_3 9.75; M 297.

* In addition to Stizolophus balsamita we investigated another two plants of the Centaurea family for their content of organic bases by the dichloroethane extraction method. Centaurea macrocephala, collected at the Sevansk Pass on July 10, 1948, contains 0.3% of total noncrystallizing bases (calculated on the dry plant); Centaurea squarrosa, collected in the Kura River valley above Akhaltsikh on July 24, 1948, contains a total of 0.12% of noncrystallizing bases.

** Viridifloric acid is prepared by saponification of the alkaloid viridiflorine [J. Gen. Chem., 18, 1736 (1948)].

Equivalent weight: 0.2072 g substance: in 20 ml water, 6.80 ml 0.1 N HCl (potentiometrically-inflection of curve at pH 5.35), equiv. wt. 304.

Specific rotation: 1.272 g substance in 10 ml water, $\underline{l}$ = 1 dm; α +3.13°; $[\alpha]_D$ +24.6°.

Stizolophine salicylate was prepared by adding an alcoholic solution of salicylic acid to an alcoholic solution of the alkaloid until the reaction was acid to methyl orange. The salt crystallized on rubbing with a glass rod; m.p. 168-169° after recrystallization from acetone.

8.020 mg substance: 0.260 ml N_2 (22.0°, 734 mm). 8.795 mg substance: 0.270 ml N_2 (21.5°, 734 mm). Found %: N 3.62, 3.44 $C_{15}H_{23}NO_5 \cdot C_7H_6O_3$. Calculated %: N 3.21.

Stizolophine viridiflorate was prepared by mixing acetone solutions of the base and viridifloric acid. The salt came down on standing and melted at 168-169° after crystallization from acetone.

8.060 mg substance. 0.228 ml N_2 (26.0°, 732.0 mm). 7.895 mg substance: 0.226 ml N_2 (27.0°, 732.0 mm). Found %: N 3.10, 3.13. $C_{15}H_{23}NO_5 \cdot C_7H_{14}O_4$. Calculated %: N 3.04.

SUMMARY

A new alkaloid, stizolophine $C_{15}H_{23}NO_5$, was isolated from Stizolophus balsamita (Lam.). The plant contains approximately 0.3% of the alkaloid.

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INVESTIGATION OF THE ALKALOIDS OF NARDOSMIA LAEVIGATA

R. S. Massagetov and A. D. Kuzovkov

Nardosmia laevigata DC. is a perennial herbaceous plant belonging to the Compositae family.

Nardosmia is a diclinous plant, throwing out floriferous stalks with yellow clusters of flowers early in the spring shortly after the melting of the snow. The leaves develop after flowering. The leaf laminae are large (15 X 25 cm), reniform, broad-crenate, perfectly smooth, located at long petioles seated on the rhizomes. The rhizome is long and creeping; in the fresh state it has a characteristic odor. The plant grows at the bottom of swiftly flowing streams and in the water close to the banks of rivers, often forming dense beds of weeds. It is found in the Altai, in the North European part of the USSR, in the Urals and in Northern Mongolia. In the Altai the plant is considered to have medicinal value. A decoction of the leaves and roots is drunk in nervous ailments and as a sedative. For the study of the alkaloids, leaves of the plant were gathered on July 21-24 at the River Malaya Ulba (Western Altai).

Although studies of the alkaloids of Nardosmia laevigata are not reported in the literature, the fact that it belongs to the Compositae family suggests the possibility that they contain alkaloids of the heliotridane series which occur in various Senecio plants of the same family. This surmise has been fully confirmed and we have been able to isolate and identify the alkaloids of the plant with relative ease. We isolated the alkaloids by the usual method of extraction of the bases with dichloroethane from the ammonia-wetted plants. We succeeded in isolating three of the alkaloids present in the plant.

Alkaloid no. 1 is insoluble in water and boiling acetone. It was purified by crystallization from chloroform and then melted at 238°; it is levorotatory: $[\alpha]_D$ −61.5° ($CHCl_3$, c 3.087). The elementary analysis indicates the formula $C_{18}H_{25}O_5N$. A comparison of the empirical formula and constants of this base with those of the alkaloid senecionine [1] indicated the possibility that they were identical. For comparison we prepared the picrate and nitrate of the base and carried out the saponification of alkaloid no. 1, isolating and characterizing the acid and the base obtained. Table 1 sets out the constants of the prepared substances and those of senecionine, its salts and hydrolysis products [1-4,8], and leaves no doubt about the identity between alkaloid no. 1 and senecionine.

TABLE 1

	Alkaloid no. 1	Senecionine	Mixed sample
Base, m.p.	238°	232°	
$[\alpha]_D$	−61.5°	−56.67°	
Picrate, m.p.	193.5°	191°	
Nitrate, m.p.	214°	214°	
Base obtained after saponification of the alkaloid, m.p.	119−120°	121−122°	119−120°
$[\alpha]_D$	+56.9°	+53.29°	
hydrochloride of this base, m.p.	163−164°	163−164°	
Acid obtained after saponification of the alkaloid, m.p.	148−148.5°	151°	148−148.3°
lactone of this acid, m.p.	155−156°	155−156°	155−156°

Alkaloid no. 2 is insoluble in water and dissolves in boiling acetone. It was separated from alkaloid no. 1 by extraction with boiling acetone and was then purified through the bitartrate. After recrystallization from acetone the base had the composition $C_{18}H_{27}NO_5$ and melted at 127-129°. After crystallization from alcohol, the bitartrate of the base had mp. 198-199° and $[\alpha]_D$ −37.6° (H_2O, c 2.099) the picrate melted at 197-198°. The composition of the second alkaloid and the constants of the base and its salts agree with the data for the alkaloid platyphylline [4, 5,6] discovered by A. P. Orekhov. We confirmed the identity between these

TABLE 2

	Alkaloid no. 2	Platyphylline	Mixed sample
Base, m.p.	127−128°	129°	127−128°
Bitartrate, m.p.	198−199°	196°	198−199°
$[\alpha]_D$	−37.6°	−38.8°	−
Picrate, m.p.	197−198°	199 200°	198−199°

substances by the absence of depression of the melting point of a mixture of alkaloid No. 2 and platyphylline or of the melting point of a mixture of their bitartrates. Table 2 contains the constants of the bases and salts of alkaloid No. 2 and of platyphylline and the melting points of the mixed specimens.

Alkaloid no. 3 dissolves readily in water, which property permitted its separation from the first two alkaloids. The base was purified by crystallization from acetone, and it then melted at 193-195°. The bitartrate melted at 210° after crystallization from alcohol. A comparison of the constants of this alkaloid with those of renardine, first discovered by A. Danilova and R. Konovalova [7] suggested identity between these two compounds, and this was substantiated by the absence of depression in the mixed melting tests with the bases and their bitartrates. Comparative data appear in Table 3.

TABLE 3

	alkaloid no. 3	renardine	mixed specimen
Base, m.p.	193 −195°	191 −193°	193 −195°
Bitartrate, m.p.	201°	198 −198.5°	199°

EXPERIMENTAL*

Isolation of the alkaloids. 22 kg air-dry plant was wetted with 10% aqueous ammonia and exhaustively extracted with dichloroethane. The alkaloids were extracted from the dichloroethane extracts with 10% sulfuric acid solution. The acid extract was treated with aqueous ammonia which brought out the water-insoluble bases (43 g); the alkaline mother liquor was extracted with chloroform. The total amount of alkaloids (19 g) obtained after driving off the chloroform was again dissolved in 30 ml 10% sulfuric acid and the solution made alkaline with ammonia. The water-insoluble bases were separated (15 g) and the mother liquor was extracted with chloroform. Removal of the chloroform left 3 g of partly crystallizing bases, soluble in water.

Alkaloid no. 1. 58 g of the total bases insoluble in water was extracted with 300 ml acetone while boiling under a reflux condenser. The insoluble residue was separated from the hot acetone extract and then recrystallized from chloroform to give 25 g product melting at 238°.

0.3087 g substance in 10 ml $CHCl_3$, $\underline{l}$ = 1 dm, α −1.90°, $[\alpha]_D$ −61.5°. 2.903 mg substance: 6.776 mg CO_2; 1.874 mg H_2O. 3.190 mg substance: 7.421 mg CO_2; 2.086 mg H_2O. 8.480 mg substance: 0.348 ml N_2 (24.0°, 728.5 mm). 8.040 mg substance: 0.308 ml N_2 (22.5°, 731.5 mm). Found %: C 63.61, 63.45; H 7.22, 7.31; N 4.52, 4.25. $C_{18}H_{25}O_5N$. Calculated %: C 64.4, H 7.45; N 4.19.

The picrate was prepared from mixed alcoholic solutions of the base and picric acid melted at 191° (from alcohol). The nitrate was prepared by acidifying the alcoholic solution of the base with alcoholic nitric acid. The salt melted at 214° after crystallization from alcohol.

Saponification of the alkaloid. 1.3 g alkaloid, 3 g barium hydrate and 15 ml water were refluxed for 8 hours, after which carbon dioxide was passed through the solution, the barium carbonate was filtered off, and the mother liquor was made acid with hydrochloric acid and exhaustively extracted with ether. The ether extract was dried with sodium sulfate and the ether distilled off to leave 0.5 g white crystalline acid which after crystallization from 25 ml dry chloroform gave 0.4 g acid melting at 148-148.5°. A mixture with senecionic acid, prepared by us by saponification of platyphylline, melted at the same temperature.

The lactone was prepared by heating 0.5 g acid for 3 hours with 10% hydrochloric acid. The solution was extracted with ether. After drying with sodium sulfate the ether was evaporated to a small volume and 0.4 g substance came down, m.p. 155-156°. A mixture with the lactone of senecionic acid melted at 155-156°. After extraction with ether, the hydrochloric acid solution was evaporated to dryness in a beaker. The crystalline residue was extracted with absolute alcohol and the solution evaporated to a small volume. Addition of ether brought down 0.4 g crystalline hydrochloride of the base which melted at 163-164°.

A mixed sample with the hydrochloride of retronecine melted at the same temperature. The base was obtained by treating the aqueous solution of the hydrochloride with sodium hydroxide until alkaline to phenolphthalein, evaporating the solution to dryness, and extracting the residue with absolute alcohol. The residual crystalline base, following evaporation of the alcohol, melted at 119-120° after recrystallization from acetone. A mixed specimen with retronecine melted at the same temperature.

0.0172 g substance in 1 ml C_2H_5OH, $\underline{l}$ = 0.5 dm, α + 0.49°, $[\alpha]_D$ + 56.9°,

* In collaboration with R. I. Bogomazova.

Alkaloid no. 2. The acetone extract after removal of the first alkaloid was evaporated to one quarter of its original volume. On cooling, it deposited 20 g base with m.p. 122-124°. The bitartrate of this base was prepared by adding a saturated alcoholic solution of tartaric acid to the alcoholic solution of the alkaloid until the reaction was acid to methyl orange. The precipitated salt melted at 198-199° after recrystallization from alcohol.

0.2099 g substance in 10 ml water, $l = 1$ dm, α −7.9°, $[\alpha]_D$ −37.6°.

The mixture with the bitartrate of platyphylline melted at 198-199°.

The base was obtained by dissolving the bitartrate of alkaloid no. 2 in water, treating the solution with aqueous ammonia, filtering the precipitate and recrystallizing from acetone. M.p. 127-128°. Mixture with platyphylline had same m.p.

3.960 mg substance: 9.250 mg CO_2; 2.927 mg H_2O. 4.070 mg substance: 9.494 mg CO_2; 3.040 mg H_2O. 9.135 mg substance: 0.346 ml N_2 (21.0, 732.5 mm). 9.155 mg substance: 0.350 ml N_2 (23.5°, 731.0 mm). Found %: C 63.71, 63.62; H 8.27, 8.35; N 4.24, 4.23. $C_{18}H_{27}NO_5$. Calculated %: C 64.1; H 8.01; N 4.17.

The picrate was prepared by mixing alcoholic solutions of the base and picric acid. After crystallization from alcohol, the salt melted at 197-198°. The mixture with platyphylline picrate melted at 198-199° (m.p. of platyphylline picrate 199-200°).

Alkaloid no. 3. 3 g of the total water-soluble bases was triturated with a small amount of acetone; the crystalline substance was filtered off and recrystallized from acetone and then melted at 193-195°. A mixture with renardine melted at the same temperature. The bitartrate was prepared by acidifying (methyl orange) an alcoholic solution of the alkaloid with an alcoholic solution of tartaric acid. M.p. (from alcohol) 201°. M.p. of mixture with renarcine bitartrate 199° (renardine bitartrate, prepared from Senecio Renardi, had m.p. 198-198.5°).

SUMMARY

Three alkaloids – senecionine, platyphylline, and renardine – were isolated from the plant Nardosmia laevigata.

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THE REACTION OF NICOTINE WITH METAL SALTS

I. REACTION OF NICOTINE WITH COBALT THIOCYANATE

S. E. Burkat

Little light is thrown in the literature on the reaction of nicotine with thiocyanates. A. A. Shmuk [1] mentions the precipitation of nicotine with solutions of potassium-platinum thiocyanate, zinc thiocyanate and calcium thiocyanate. The author did not state the composition and properties of the reaction products. In the present author's recent publication [2] it was shown that nicotine and its salts give in presence of ammonium thiocyanate readily crystallizing, characteristic precipitates with salts of nickel, cobalt, manganese and other metals. The composition and character of the obtained compounds were not established. In view of the general chemical interest of these compounds, we have made an investigation of their composition and of some of their properties.

Little attention has been given to the composition of the products of reaction of nicotine with salts of various metals. Nicotine is a strong organic base and when added to solutions of salts of heavy metals it precipitates their hydroxides [3]. Some of the qualitative reactions for nicotine are similar to those for pyridine, evidently due to the presence of the pyridine ring in the molecule [4]. It is known that pyridine in presence of ammonium thiocyanate forms with cadmium and copper salts complexes that are sparingly soluble in water [5]. We might assume nicotine would also form complex compounds in the same conditions. This property was indicated by A. A. Shmuk. The same author points out, however, that little attention has so far been given to the complex compounds of nicotine with bismuth, mercury and other metals. On the other hand, a number of authors describe the ease with which nicotine forms double salts with various metals [6,7]. In a number of cases nicotine yields compounds of variable composition with metal salts.

Our investigation of the preparation, composition and properties of compounds of nicotine with cobalt thiocyanate showed that addition of a solution of complex cobalt thiocyanate to an aqueous solution of nicotine or of its salts gives an amorphous precipitate with a light-to-dark-blue color, which rapidly changes into a pink, crystalline precipitate. The reaction product can be readily recrystallized from water at the boil.

The product has a sharp melting point (with partial decomposition), is sparingly soluble in cold water and more soluble on heating. It has slight solubility in ethyl alcohol in the cold and rather better solubility in hot alcohol, forming a dark-blue solution. It is not appreciably soluble in ether, chloroform, dichloroethane and benzene. With the help of common reagents the presence of ions of cobalt and thiocyanate and of nicotine was readily established in the saturated aqueous solution. The aqueous solution of the substance titrates with caustic alkali, indicating that nicotine is present in the form of a salt. Analyses revealed that the compositions of the compound prepared from nicotine base and from its salts were constant. All these facts point to the formation of a double salt of nicotine with Co thiocyanate and not of a complex compound.

EXPERIMENTAL

We isolated the nicotine for the investigation from technical nicotine sulfate by extraction with ethyl ether in presence of caustic alkali followed by steam-distillation. Nicotine was extracted from the aqueous solution with ethyl ether and the solvent was removed in the usual way.

Preparation of double salt of nicotine thiocyanate and cobalt thiocyanate. 2.25 g crystalline cobalt nitrate $Co(NO_3)_2 \cdot 6H_2O$ is dissolved in 5 ml water. In a separate vessel a solution is prepared of 5 g ammonium thiocyanate in 5 ml water and the two solutions are mixed. Into a 200 ml flask is introduced 2.5 g nicotine (base), 50 ml water is added and the liquid is neutralized with 25% hydrochloric acid (using methyl red as indicator). The solution of the cobalt thiocyanate complex is energetically stirred into the nicotine solution and the mixture is stood for 15 minutes. At first an amorphous light-to-dark-blue precipitate is formed which changes into a pink, crystalline one. This is drained and dried at room temperature. Yield of technical

product 4.30 g or 90.3% of the theoretical if we assume that the compound is formed according to the following equation:

$$2C_{10}H_{14}N_2 \cdot HCl + Co(NO_3)_2 \cdot 6H_2O + 4NH_4CNS = (C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2 + 6H_2O + 2NH_4NO_3 + 2NH_4Cl.$$

Melting point of the technical product 194-196°.

The technical product is dissolved in 60 ml water by boiling, and the solution is filtered without delay under reduced pressure. Rapid separation occurs of a dark-to-light-blue mass which quickly changes into pink crystals. After cooling to 15°, the crystals are drained on a Buchner funnel and again recrystallized from 40 ml water at the boil. The crystals are dried between sheets of filter paper at room temperature. Yield of pure product 2.20 g, m.p. 199-200°.

Subsequent experiments showed that: 1) The synthesis of the preparation is better performed with a solution of a nicotine salt since addition of the complex cobalt thiocyanate to the nicotine-base solution results in a pink, crystalline precipitate which contains light-to-dark-blue particles; the greater the dilution of the nicotine solution the lower the yield of reaction product; 3) with increasing acidity of the medium of the solutions, the yield of reaction product falls.

The prepared compound is a dark-pink crystalline substance. Solubility in water at 15° is 0.35%. Aqueous solutions are colored pink. The compound dissolves in normal inorganic acids, with difficulty in acetic acid. It dissolves without any special characteristics in concentrated sulfuric, nitric and hydrochloric acids. Precipitates characteristic of cobalt are formed when caustic alkali, ammonia and ammonium sulfate are added to the aqueous solution of the prepared compound. The reactions with potassium ferro- and ferricyanides are not quite typical of those for cobalt. Instead of the typical brownish-red precipitate given by cobalt with potassium ferrocyanide solution, there is formed a greenish precipitate which fairly quickly changes to dirty-blue. With potassium ferricyanide solution the aqueous solution of the compound gives a green precipitate.

With common alkaloid reagents the aqueous solution of the prepared compound gives the precipitates typical of alkaloids. Addition of iron chloride to the aqueous solution of the compound causes a blood-red coloration; addition of silver nitrate brings down silver thiocyanate.

Cobalt was quantitatively determined in the preparation by the gravimetric method in the form of sulfate. Nicotine was determined by steam distillation in presence of alkali and common salt, followed by titration with 0.1 N hydrochloric acid (methyl red as indicator). Quantitative determination of the thiocyanate ion was performed with a saturated aqueous solution of the compound by the argentometric method.

0.5000 g, 0.4860 g, 0.5050 g substance: 0.1320 g, 0.1214 g, 0.1280 g $CoSO_4$. 0.3124 g, 0.5000 g, 0.2560 g substance: 19.72 ml, 32.46 ml, 16.61 ml 0.1 N $AgNO_3$. 0.2388 g, 0.2522 g, 0.2500 g substance: 7.40 ml, 7.90 ml, 7.65 ml 0.1 N HCl. Found %: Co 10.02, 9.48, 9.62; CNS' 36.61, 37.65, 37.62; nicotine 50.33, 50.74, 49.57. $(C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2$. Calculated %: Co 9.54; CNS' 37.64; nicotine 52.50.

Determination of the thiocyanic acid combined with the nicotine was performed by titration of the aqueous solution of the compound with 0.1 N sodium hydroxide in presence of phenolphthalein. Since the aqueous solution of the substance is colored pink, the volume taken for the titration is diluted with water until the color disappears.

0.3024 g, 0.2522 g, 0.1604 g substance: 9.60 ml, 7.90 ml, 5.10 ml, 0.1 N NaOH. Found %. HCNS 18.73, 18.47, 18.75. $(C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2$. Calculated %: HCNS 19.13.

SUMMARY

The double salt of nicotine thiocyanate with cobalt thiocyanate was prepared. Its composition and properties have been studied and it has been shown to correspond to the formula $(C_{10}H_{14}N_2)_2 \cdot 2HCNS \cdot Co(CNS)_2$.

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PIRYLENE

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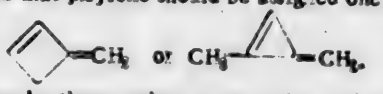
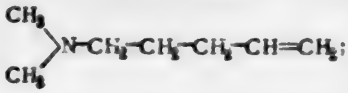
In 1888 a hydrocarbon of the composition C_5H_8 was first synthesized and given the name of "pirylene". Its structure has remained unestablished up to now. Originally it was assigned the structure of cyclopentadiene [1]. Later it was entered in the handbook literature as a hydrocarbon of the aliphatic series of unestablished structure [2]. Later, on the basis of a study of the molecular refraction, Braun and Teuffert [3] arrived at the conclusion that pirylene should be assigned one of the following two structures:

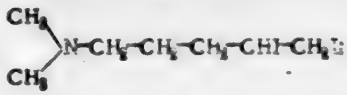


Oxidation of pirylene by these authors gave oxalic acid and acetic acid. In presence of palladium the hydrocarbon combined with 4 atoms of hydrogen. These data are inadequate for making a choice between the alternative structures. The authors refrained from selection of one of them.

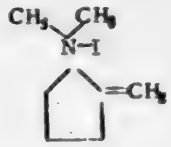
The starting material for the preparation of pirylene is piperidine. Exhaustive methylation of the latter gives des-N-dimethylpiperidine (I). Reaction of this with alcoholic iodine solution with iced-water cooling converts it quantitatively into the diiodo compound (II). Short-period heating of the latter with caustic alkali causes cleavage of one molecule of hydrogen iodide and intramolecular rearrangement takes place to form a pyrrolidine derivative (III) whose structure has been fairly satisfactorily established [4,5,6]. Treatment of this compound with silver oxide leads to a free quaternary base which decomposes when heated and forms the so-called dimethylpiperideine whose structure was not established. Braun and Teuffert [3] suggest that this amine contains either a cumulated or an isolated system of double bonds, (IV, V). Dimethylpiperideine is unstable. It readily resinifies when kept. Its methiodide decomposes when heated with caustic alkali and forms the hydrocarbon pirylene. It is interesting to note that the yield of hydrocarbon is negligible when the alkali is replaced by silver oxide.



(I)



(II)



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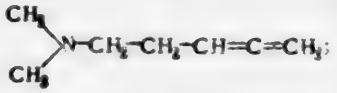
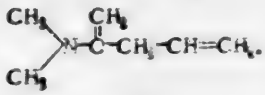


(IV)



(V)

In the present investigation pirylene was synthesized in the precise conditions described in the literature [1,3,6]. The yields of the hydrocarbon and intermediate products agreed with those in the literature. The prepared hydrocarbon differed somewhat in physical properties from the hydrocarbon of Braun and Teuffert. M.p. 57-58°.

d_4^{20} 0.7412; n_D^{20} 1.45797; MR_D 24.29. C_5H_8. Calculated: MR_D 22.82. Exaltation 1.47.

The hydrocarbon does not react with reagents for monosubstituted acetylenes. Hydrogenation over platinum black causes addition of 6 hydrogen atoms. Consequently, contrary to the statements of Braun and Teuffert, pirylene must contain either three double bonds (very improbable) or a double and a triple bond.

Raman spectra were plotted to assist in the elucidation of the structure.

$\Delta\nu$: 238 (3), 259 (3 w), 319 (3), 261 (2), 397 (2), 422 (2), 468 (5), 518 (5), 548 (2), 658 (2), 678 (1), 703 (2), 732 (2), 791 (1), 869 (1), 913 (1), 1029 (1), 1082 (8), 1106 (1), 1163 (10), 1276 (2), 1295 (6 w), 1380 (5), 1412 (8), 1559 (1), 1586 (1), 1609 (10), 1618 (5), 1936 (4), 2098 (1), 2137 (1), 2189 (4), 2237 (10), 2339 (1), 2860 (1), 2889 (1), 2921 (8), 2984 (4), 3013 (3), 3099 (2).

We see from the above data the the pirylene spectrum contains a series of frequencies both in the

1600 cm^{-1} region and in the 2200 cm^{-1} region. This confirms that pirylene contains both a double and a triple bond. The low value of the frequencies of the double bond (1609 and 1618 cm^{-1}) shows that the double bond is at the end of the hydrocarbon chain and is also conjugated.

The frequency of the triple bond (2237 cm^{-1}) shows that the acetylene is disubstituted.

On the basis of the foregoing data we can assign to pirylene the structure $CH_3-C\equiv C-CH=CH_2$.

This structure accords well with the above-mentioned oxidation products.

In this connection it was of interest to clarify the structure of dimethylpiperideine. Spectroscopic examination of this amine was made very difficult by the ease of resinification of the free amine and its high sensitivity to irradiation.

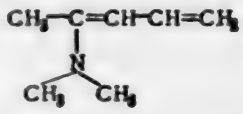
The freshly distilled amine had b.p. 73-75° (100 mm).

d_4^{20} 0.8024; n_D^{20} 1.4618; MR_D 38.01. $C_7H_{13}N$. Calculated: MR_D 37.53.

Raman spectrum of the amine: 290 (2), 341 (1), 855 (1), 909 (1), 962 (1), 1020 (1), 1049 (1), 1124 (3), 1191 (1), 1229 (3), 1266 (1), 1309 (3), 1374 (5), 1411 (2), 1439 (2), 1458 (4), 1504 (2), 1531 (3), 1596 (4), 1650 (20), 2232 (2), 2313 (1), 2491 (3), 2880 (2), 2921 (1), 2989 (1).

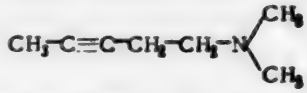
The spectrum contains frequencies of 1596 and 1650 cm^{-1}. The latter have an extraordinarily high intensity. This permits us to conclude that dimethylpiperideine contains a conjugated system of double bonds. Also the presence in the spectrum of the frequency 2232 cm^{-1} with a low intensity indicates that dimethylpiperideine is not a pure substance but is contaminated with a small amount of an amine containing a β-acetylenic bond. The amount of the latter may be estimated at 10-15%.

It follows from the spectroscopic data that the main component of dimethylpiperideine must be assigned the structure:



Exhaustive methylation of this amine should lead to formation of a hydrocarbon with a conjugated acetylenic-ethylenic bond.

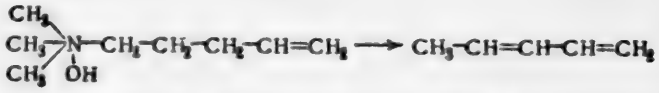
The byproduct present in dimethylpiperideine must be assigned the structure:



Exhaustive methylation of this amine leads to formation of the same hydrocarbon with a conjugated acetylenic-ethylenic bond.

Consequently, the opening of the pyrrolidine ring (III) in the present case is accompanied by isomerization which leads to formation of a hydrocarbon with a conjugated system of bonds.

Isomerization during exhaustive methylation was observed for the first time in the classical synthesis of piperylene. In this case, instead of a hydrocarbon with isolated bonds, formation takes place of piperylene containing a conjugated system of bonds [7]



We prepared piperylene by exhaustive methylation of des-N-dimethylpiperidine. In the spectrum of this hydrocarbon the frequencies 1596 and 1645 cm^{-1} correspond to a conjugated system of double bonds. It was of interest to compare the frequencies of the conjugated bond system of this piperylene with the frequencies of the conjugated system of the same hydrocarbon prepared by other methods. In the preceding communication [8] we showed in collaboration with I. N. Shokhor that the spectrum of piperylene prepared by regeneration from its crystalline tetrabromide with m.p. 114.5° contains four double-bond frequencies: 1596, 1603, 1646 and 1655 cm^{-1}. The suggestion was made that these frequencies, taken in pairs, correspond to the cis-form (1596 and 1646 cm^{-1}) and the trans-form (1603 and 1655 cm^{-1}).

The same four frequencies were found in the spectrum of piperylene prepared from its liquid tetrabromide; however, two of them (1603 and 1655 cm^{-1}) were much more intense than the others. Bearing in mind that the trans-form must be characterized by higher frequency values than the cis-form, it had to be assumed that the trans-form predominates in piperylene prepared from the liquid tetrabromide. The data obtained in the present investigation show that exhaustive methylation of des-N-dimethylpiperidine gives exclusively cis-piperylene (frequencies of 1596 and 1645 cm^{-1}). The spectrum of the pure trans-piperylene might be expected to contain only the frequencies 1603 and 1655 cm^{-1}. This was confirmed by examination of piperylene prepared by cleavage of hydrogen chloride from α-chloroethylcyclopropane [8].

The table contains the data for the Raman spectra of the above four specimens of piperylene.

Raman Spectra of Piperylene Prepared			
by exhaustive methylation of des-N-dimethylpiperidine	from the crystalline tetrabromide	from the liquid tetrabromide	by cleavage of HCl from α-chloroethylcyclopropane
386 (5)	386 (5)	386 (5)	386 (3)
478 (2)	478 (5)	478 (5)	478 (4)
618 (1)			
	814 (1)	816 (1)	816 (5)
899 (2 w)	897 (4 w)	897 (3 w)	898 (4 w)
952 (2)	955 (1)	955 (1)	
1034 (1)	1032 (1)	1034 (1)	
1106 (0.5)			
1167 (3)	1174 (3)	1172 (3)	1174 (3)
	1183 (7)	1184 (6)	1188 (10)
1191 (1)			
1248 (10)	1250 (8)	1248 (6)	1248 (2 w)
1296 (8)	1292 (10)	1290 (10)	1292 (8)
		1324 (1)	
1388 (2)	1376 (6)	1376 (5)	1379 (2)
	1413 (5)	1413 (4)	1413 (2)
1435 (4)	1432 (3)	1434 (2)	1430 (5)
1468 (4)	1451 (6)	1451 (6)	1451 (5)
1596 (3)	1596 (4)	1596 (0)	
	1603 (4)	1602 (6)	1603 (1)
1645 (10)	1646 (10)	1646 (2)	
	1655 (10)	1655 (10)	1655 (10)

SUMMARY

1. Pirylene is 1-Penten-3-yne.

2. The main component is dimethylpiperideine is 4-dimethylamino-1,3-pentadiene. It contains an impurity in the shape of 1-dimethylamino-3-pentyne.

3. The hydrocarbon formed by the exhaustive methylation of des-N-dimethyl-piperidine is cis-piperylene.

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DISCUSSION

THE STATE OF THE THEORY OF CHEMICAL STRUCTURE IN ORGANIC CHEMISTRY

B. A. Kazansky and G. V. Bykov

The creative development of A. M. Butlerov's theory of chemical structure is the main task now confronting Russian chemists in the field of theory. Dialectical materialism—the methodological basis of Soviet science—requires the study of phenomena and their cause, movement and change. Consequently without an historical approach to the subject matter of the basic concepts and laws of the theory of chemical structure, it is impossible to detect the profound conceptual changes in them or the tendencies that are inherent in their development at the present day.

At the Conference on the Theory of Chemical Structure organized by the Division of Chemical Sciences of the Academy of Sciences in June, 1951, the idealistic theory of resonance or mesomerism was rightly subjected to annihilating criticism. There was thus removed a fundamental obstacle to the fruitful development of the theory of organic chemistry, a development that would be impossible without creative discussions, without the clash of ideas, without criticism and self-criticism. In order, however, that the creative discussions of our chemists should be fruitful, we must make a critical evaluation of the relevant problems without any polemic sophistics that would hinder the objective clarification of controversial topics.

We believe that in the first place we must exchange ideas on the following fundamental problems: 1) Modern ideas on chemical structure; and 2) the modern approach to the relation between properties and structure of organic compounds. As was revealed at the Conference on the Theory of Chemical Structure, there are many different, frequently incompatible, points of view in connection with each of these questions, and it is here that agreement between Soviet chemists is particularly necessary.

I

Scientific concepts change, being enriched by new content as science reflects more and more fully and accurately the field of objective reality that it explores. This implies that we must base the modern content of chemical structure on the history of our knowledge of the structure of molecules.

According to the theory of radicals—the first theory of organic chemistry—organic compounds consist of relatively autonomous parts (complex radicals). The various modifications of the theory of radicals, dualistic in principle, were more or less closely associated with the electrochemical hypothesis. All of them came into direct conflict with experiment and were abandoned in the fifties of last century. Dumas replaced them by his theory of types, according to which the substances possessing the same number and distribution of atoms belonged to one and the same mechanical type (mechanical system). At that time, of course, chemists could not visualize a spatial distribution of atoms, although many unfounded hypotheses were put forward, based mostly on crystallographic analogies and the study of specific volumes. A reaction to the current ideas was Gerhardt's declaration that chemical methods of investigation are inadequate for evaluation of the "molecular constitution of substances, i.e. the actual arrangement of their atoms". Gerhardt's types, unlike those of Dumas, were solely intended to express the reactivity of organic compounds. Berthollet proposed to characterize organic compounds by equations of formation (genetic equations), free from any hypotheses and simply expressing the facts. This was the standpoint of extreme empiricism and it erred in that chemical concepts and theory are able to reflect true actuality. This approach was only an attempt at systematization; the theory was judged solely from the standpoint of its expediency. Philosophical agnosticism was the methodological basis of this trend in chemistry.

The concepts of types had a positive value insofar as they led to two important generalizations: to the concept of atomicity (valence) of elements or of a specific number of units of affinity; and, second: to the concept of the linking of atoms with one another through the "expenditure" (Butlerov's term) of an even number of units of affinity. At that time, of course, there could be no discussion of the nature of units of affinity or of

the interatomic bond. There was still no clear demarcation between the spatial arrangement and the mutual atomic linkage, and the term "constitution" began to lose its original specificity. The absence of a generalization that could integrate the advances of theoretical chemistry hindered its further development. It was A. M. Butlerov who supplied this generalization in the form of the concept of chemical structure: "Starting from the idea that each chemical atom entering into the composition of a substance takes part in the formation of that substance and acts here with a definite amount of its inherent chemical force (affinity), I call chemical structure the distribution of the action of this force, due to which the chemical atoms, directly or indirectly influencing• one another, become combined into a chemical particle" [1]. Subsequently, Butlerov more laconically defined chemical structure as "the order of chemical bonding existing between atoms in a molecule" [2]. Hence the concept of chemical structure as well as of the order of mutual bonding of atoms in a molecule was the natural result of the whole previous development of science. In the words of Butlerov, "historical necessity led to the theory of chemical structure" [3].

In formulating the concept of chemical structure A. M. Butlerov turned away from the idea of the mechanical structure of molecules. The necessity for this new path was acutely recognized by him. On the one hand, as he wrote, "chemistry, being concerned with matter in a state of transformation, cannot without the help of physical investigations evaluate the mechanical structure of substances" [4], and the possibilities of physical methods of investigation at that period in history were still inadequate for the evaluation of the spatial distribution of atoms, although Butlerov often emphasized that the spatial distribution of atoms would in the future also be amenable to determination: on the other hand, chemists still did not know "of that bond which exists inside the molecule between the mutual chemical action of the atoms which constitute it and their mechanical distribution" [4], while the "chemical properties of the molecule are regarded predominantly as the chemical behavior of the constituent atoms" [4] i.e., its chemical structure. The latter view received spectacular confirmation in the clarification of numerous cases of isomerism: "The principle of chemical structure", said Butlerov, "leads to the a priori assumption of the existence of known isomers" [5]. In the course of time, however, chemists became convinced that the number of actually existing isomers, corresponding to a given empirical formula, exceeds the number of isomers possible on the basis of the theory of chemical structure. The facts compelled them, in the words of Wislicenus [6], "to explain the diversity of isomeric molecules with an identical structural formula by a different arrangement of their atoms in space and to search for definite theories about this arrangement". V. V. Markovnikov voiced the same ideas [7]: "Concerning the grouping of atoms, it (the theory of structure) can in no way wish to touch on the problem of the relative spatial arrangement of atoms.... That is why the former expression "constitution" had to be replaced by the term "chemical structure"... It is difficult, however, to conceive that there do not exist direct and specific relationships between the chemical interaction and physical position of the atoms in the molecule. Finally, there exist certain circumstances, certain facts, which point very strongly to the existence of such relationships. What precisely these are we cannot yet say, but this is one of the most pressing problems which must be solved by some means or other". Two years after these remarks, the first publications of van't Hoff and Le Bel on stereochemistry appeared—the doctrine of the relative position of atoms in space. The perfecting of physical methods of investigation has permitted in our time the determination of the equilibrium interatomic distances and valence angles in absolute units. Chemists are now in a position to study the geometry (or as A. M. Butlerov said, the mechanical structure), of molecules and have thus scored a fresh success for the theory of chemical structure.

But the solution of the problem of molecular geometry has left many problems still unsolved. Foremost among these are the reactivity of organic compounds, the generalization of the accumulated experimental material, and the discovery of the mechanism of reciprocal influence of atoms in a molecule. Still unclarified is the nature of valence and the chemical bond, on the understanding of which rests the classical theory of chemical structure. The discovery of the electron and of the theory of atomic structure have in large measure led to a solution of these problems. The role of valence electrons in interatomic bonds has been cleared up: quantum mechanics has accounted for the direction of bonds in space and for their saturation and has introduced the ideas of the electron cloud with an irregular electronic "density" of the difference between σ- and π-electrons, of the differing arrangement (and properties) of the σ- and π-electronic density and of the electronic density of the inner shells of the atom. All this signifies another step forward in the understanding of the structure of molecules.

• We may note that Butlerov often used the word "influence" in the sense of "bond" or "union" of atoms and his term was translated, as in the present case into German by the words "Zusammenhang" or "Bindung", but strictly the Russian word for "influence" is rendered in German by "Einfluss".

At the present time, consequently, the concept of chemical structure of molecules embraces the ideas of the order of combination of atoms among themselves, of the position of atoms (nuclei) in space, i.e. of the geometry of molecules, and of the distribution of electron density in molecules*.

We are of the opinion that such a concept of the chemical structure is most in harmony with the history and contemporary ideas of the structure of molecules. It is natural that further progress in the field of the structure of matter will enrich the content of the theory and render it more precise.

II

The mechanical types of Dumas showed with particular clarity the attempts of chemists to express the functional dependence of the properties of chemical compounds on the spatial distribution of the atoms. Kekule wrote in 1859 that "the relative position (relative Stellung) of individual atoms has a definite influence on the nature of compounds" and that although it is impossible to present a proved theory of the nature of the relative position, the existence of such an influence was clearly reflected in "the difference of properties of compounds possessing the same composition", i.e. isomers. This very faulty concept of the exclusive dependence of the chemical properties of compounds on the relative position of their atoms divided the great majority of the chemists of his day.

It is therefore impossible to deny the enormous revolutionary significance of the above-enunciated theory of A. M. Butlerov to the effect that "the chemical properties of a molecule are predominantly governed by the chemical interplay** of the component elements" [4]. This idea is expressed still more clearly by Butlerov in the words: "The well-known rule that the nature of a molecule is governed by the nature, number and arrangement of the elementary component parts should now, in my opinion, be changed to the following form: The chemical nature of a molecule is governed by the nature of the elementary component parts, their number and their chemical structure" [9]. Butlerov thus formulated to his contemporaries the following policy ("...we shall concern ourselves only with those problems which can be solved by chemical experiment [9]): The investigation of the chemical structure of substances with the help of chemical reactions." Work along these lines also released organic chemistry from the "awkward" position which it occupied at the beginning of the sixties of last century. A direct consequence of this "law" is the clarification of isomerism: Insofar as the chemical properties ("chemical nature") of substances depend on composition and chemical structure, for a given composition any difference in properties will be the result of differences in chemical structure. This law was the source of the first ideas and of the entire theory of the mutual influence of atoms in molecules: two isomers possess different properties and constitute two different substances "because the chemical relation of the atoms to one another is not the same in both molecules" or in other words "because the individual atoms of one and the same element in both molecules are not equivalent. Two, in themselves, identical and equivalent atoms consequently become nonequivalent due to the difference...in the influence of the other atoms present in the same molecule" [10]. Finally it was this very law that invested chemical structural formulas with profound significance: "...when the general laws of the dependence of chemical properties on their chemical structure become known, then such a formula will be the expression of all these properties" [11]. There cannot be any doubt that this Butlerov law is a focal point in the theory of chemical structure as it was propounded in Butlerov's statement of 1861. It binds together all the remaining ideas and concepts of Butlerov's theory and without it the concept of chemical structure itself would have remained suspended in mid-air. In putting forward his "law" he wrote: "I am far from claiming that this law is completely true and that it adequately expresses all the conditions on which the properties of compounds depend... the later development of the opinion here put forward will show to what exent chemical properties depend on chemical structure and to what extent the propounded law is inadequate..." [9]. Actually in the later study of organic compounds it became clear that the above law is not always valid, and this fact led as mentioned above, to the development of stereochemistry, the study of the dependence of properties on the mutual arrangement of atoms in space. But the latter doctrine was able to develop by the study not only of chemical properties such as the order of chemical

* Historically the term "chemical structure" was understood to be restricted to the order of combination of atoms with one another (sequence or arrangement of the bonds) in the molecule which Butlerov always clearly differentiated from the spatial arrangement of atoms. This is chemical structure in its original significance. Nor did Butlerov include the composition ("nature and number of elementary components") of the molecule in the concept of chemical structure it is obvious that even today there is no need to widen the concept in such a way, since when speaking of chemical bonds chemists always understand the linkages between specific atoms.

** In the German text the term "chemischer Zusammenhang" is used.

bonds in molecules, but also of physical properties (e.g. rotation of the plane of polarization). It is due solely to physical investigations that it became possible to characterize quantitatively the direction of bonds in space. With regard to the study of electronic structure, chemical methods differ from physical methods (study of dipole moments, molecular spectra, energies of formation and transformation, etc.) in being able to supply only indirect information. The importance of physical methods of investigation of molecular structure continuously grows. Not a single contemporary hypothesis relating to the electronic structure of molecules could be considered well-founded if it ignored or contradicted the data of physical methods of investigation.

Consequently, Butlerov's law, while almost entirely retaining its original formulation (the nature of molecules is governed by their composition and chemical structure) acquires ever wider significance since the nature of molecules embraces both their chemical and physical properties, while chemical structure involves the order of addition of atoms, the geometry of molecules and the distribution of the electronic density. Many-sided study of the relation between properties and structure with the objective of discovering the relevant laws must, it appears to us, be the main route to further creative development of the theory of chemical structure in organic chemistry. This route, just as in the time of A. M. Butlerov, is bound to lead to new advances in our understanding of the structure of organic compounds, and will permit practical solution of the important problems of better utilization of already known compounds and the preparation of new compounds with made-to-measure properties.

III

In the volume entitled "A. M. Butlerov. Collected Studies in Organic Chemistry"* appeared our paper on "A. M. Butlerov and the theory of chemical structure". The main purpose we had in mind when writing that paper on the work of Butlerov was to answer the question: "How did the theory of chemical structure arise and develop and what part was played by A. M. Butlerov?" [12]. In this connection we gave a detailed comparison of the publications of A. M. Butlerov with those of his predecessors and contemporaries, and it was clear from this comparison that the priority in the creation of the theory of chemical structure belongs to our great chemist. We strove to help the reader to become familiar with the content of Butlerov's theoretical studies as expounded in the volume. Finally, we wished to fill a gap left by historians of chemistry by giving an account of his battle as a natural materialist and dialecticist against agnostic and mechanistic attacks on the theory of chemical structure. We believe that we were able to publish in the paper new facts and to examine the situation from a new angle in the light of these new facts. We paid least attention to the modern significance and content of the theory of chemical structure. We decided that it would be out of place to expound our standpoint regarding contemporary problems of the theory of chemical structure in our paper accompanying the researches of Butlerov, a series devoted mainly to the origin and to the first Butlerov period of development of the theory of structure. In our paper, therefore, we did not give a detailed analysis of the present-day content of the concept of chemical structure, although we did point out some new facts about the modern concept for comparison with Butlerov's classical definition. Our comments on this score, as well as our whole paper, were severely criticized by G. V. Chelintsev [13]. We leave the readers to judge whether this criticism was justified.

At the start of his paper G. V. Chelintsev quotes our words. "Naturally the theory of chemical structure did not fully retain its original classical form and was subject to further development. Although A. M. Butlerov considered it necessary to limit the concept. . . of the chemical structure and spatial distribution of atoms while imparting a provisional character to this limitation (our italics. G. V. Chelintsev replaced these words by a row of dots —Authors' note), it has long lost its significance for the modern theory of structure. When a modern chemist speaks of the structure of a molecule of an organic compound, he uses the word in the literal sense. i.e. he has in mind the spatial...distribution of the atoms which compose it...the specific polarity of its component parts, etc." [14]. Of course it is permissible to add that the modern chemist is not limited by this, as is evident from the two paragraphs following the quotation by G. V. Chelintsev, but it is impossible to deny

* As the editors of the volume, we take this opportunity of drawing readers' attention to errors that came to light after publication: On p. 104, line 2 from bottom for "ethylene oxide" read "ethylidene oxide"; p. 112. line 10 from bottom. for "proposed" read "proposal"; p. 225, line 14 from top, for "always" read "of all"; p. 533. lines 4-3 from bottom. for "alkali metals and especially silver" read "the majority of metals"; same page. line 3 from bottom, the word "majority" is to be lowered; p. 675, line 3 fromtop, for "155" read "248".

that stereochemistry was a necessary deepening of the classical theory of chemical structure; it is impossible to say that the modern chemist does not have in mind the spatial arrangement of atoms when speaking about the structure of a molecule, etc. Without considering our remarks on the matter, G. V. Chelintsev there and then rushes to the attack: "Hence (?) the concept of chemical structure of A. M. Butlerov, which according to B. A. Kazansky and G. V. Bykov fundamentally distinguishes the teaching of Butlerov from the views of Kekulé and Kolbe (p. 563) is declared —from the standpoint of modern chemists —to be erroneous". We wish to point out that on p. 563("A. M. Butlerov. Selected Works ") in general nothing is said about the fundamental distinction between the doctrine of Butlerov and the views of Kekulé and Kolbe or that the fundamental difference between them consists mainly not in the problem of the approach to the spatial position of the atoms, although Butlerov was more optimistic about the feasibility of his concept than were the German chemists. On the point that the teaching of Butlerov was both materialistic and dialectic, we would say that the views of Kekulé and Kolbe were characterized by the agnosticism which is erroneous in the light of dialecticism; Kekulé was also tainted by eclecticism. Having assailed us with the help of only one "hence" on the score that we consider Butlerov's theory of chemical structure to be erroneous, G. V. Chelintsev goes on to attribute directly to us the following statement: "At the end of the second of the above citations from the paper by Kazansky and Bykov it is stated that although Butlerov's concept of chemical structure was erroneous, it..." [15], etc. In the paper in question*, however, there is not the least hint to the effect that "Butlerov's concept of chemical structure was erroneous". Or: "B. A. Kazansky and G. V. Bykov refer to the fact that the erroneous (!) concept of chemical structure of A. M. Butlerov..." [15], etc. He then goes on in the following style: "In their paper Kazansky and Bykov regard the theoretical concept of A. M. Butlerov as some collection of opinions devoid of a clear logical connection" [15]. We consider it necessary to explain that this statement completely contradicts the whole content and tenor of our paper and we must protest against the shamelessness with which Chelintsev converts white into black.

Chelintsev, as well as other like-minded Soviet chemists, frequently attributes to us erroneous, and sometimes even simply nonsensical, statements in order to create a target for his attacks. Here is one example. G. V. Chelintsev writes: "A red thread through the whole career of A. M. Butlerov...is the idea of the decisive significance of a supermechanical law in chemical phenomena. To say, as do Kazansky and Bykov, that this idea possesses a secondary significance in Butlerov's theory of chemical structure is a gross perversion of the teaching of A. M. Butlerov" [15]. Elsewhere [16] G. V. Chelintsev states that we regard this "idea" as simply fallacious. We are bound to point out that nowhere in our paper is there mention of the significance of the idea of a "supermechanical" law in Butlerov's theory; on the contrary, we differ from the author of "the new structural theory" in not considering ourselves entitled to ascribe to A. M. Butlerov any "ideas" that he did not enunciate.

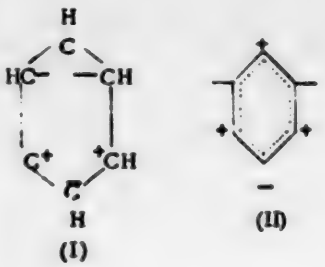
G. V. Chelintsev also attributes to us such statements as: "now Butlerov's concept of chemical structure is equivalent to the concept of arrangement of atoms in space" [17]; it is alleged that we regard molecules as "certain mechanical aggregates of electrons and nuclei" [17] that "in the light of modern science the concept of chemical structure resolves itself into the concept of a mechanical state" [17]; that "modern chemical science treats the mechanical concept of chemical structure only as the spatial location of atoms in molecules", and so on. In short, G. V. Chelintsev attributes to us the statement that the arrangement of atoms in molecules is governed by the mechanical interaction of the atoms, i.e. he attributes to us the view that prevailed in the second half of the past century. Actually, we, like the overwhelming majority of contemporary chemists and physicists, have in mind —when speaking of the arrangement of atoms in space —an atomic interaction of an electromagnetic character.

We have cited examples of the polemic imagination of G. V. Chelintsev not so much to reconstruct

* We reproduce in full the citation to which Chelintsev alludes and which was artificially made up by him from two disconnected passages taken from different pages "The concept of chemical structure is nevertheless not basic to Butlerov's theory. The central place in it is occupied by his theory of the dependence of the chemical properties of a compound on its structure" (p. 569) . . . however, the Butlerov concept of chemical structure was an essential step forward since...by drawing a distinction between the concept of arrangement of the bonds of chemical atoms and the concept of the arrangement of physical atoms in space ("the relative arrangement of the atoms"), it expressed the true purpose of the development of organic chemistry —the establishment of the chemical structure of organic compounds" (p. 558).

for ourselves the "superlogic" of the attacks made on us by Chelintsev (which is obvious to everybody acquainted with our paper on "A. M. Butlerov and the theory of chemical structure"), as with the objective of showing that sophistry in its crudest form, especially the arbitrary interpretation of citations already commented on by A. N. Nesmeyanov [18], is a favorite weapon of the author of "the new structural theory", both in attacks on others and in defense of his theoretical concepts, about which latter we have something to say below.

As we know, the central concept of Chelintsev's "new structural theory", unanimously rejected by Soviet chemists and physicists (see the transcribed report of the Conference on the Theory of Chemical Structure) is the concept of the homeopolar electrovalent bond. He writes: "The orbit-contact formulas of benzene, ethylene, naphthalene, anthracene, etc. only appear possible in the light of the concept of the homeopolar electrovalent bond" [19], or "In order to be able to write...the formula of benzene, I foresaw (?) the possibility of the homeopolar electrovalent bond" [20]. Actually, without this concept the whole "new structural theory" would not have represented anything original. As far back as 1923, Lowry [21] put forward the suggestion that "whereas a single bond may be either covalent or electrovalent, a double bond in organic chemistry usually reacts as if it consists of one covalent and one electrovalent bond...their existence can be justified on the basis of the electronic theory of valency by assigning a complete octet to each negatively charged atom and a sextet of electrons to each positively charged atom". Lowry represented butadiene by the formula $\overset{+}{C}H_2-\overset{-}{C}H\ \overset{+}{C}H-\overset{-}{C}H_2$, and pointed out that according to his scheme "the distinction between a single and a double bond in conjugated systems disappears completely". Lowry's benzene formula (I), the formulas of butadiene and a series of other compounds differ from the corresponding formulas of Chelintsev [22]: $\overset{+}{C}H_2-\overset{-}{C}H-\overset{+}{C}H-\overset{-}{C}H_2$ and (II), "which express the close multiple bonds of conjugated systems" [23] only by the absence of the dotted line indicating the electrovalent bond. Lowry's formulas have long disappeared from the stage. G. V. Chelintsev tries in vain to infuse new life into them. He writes: "The origin of alternating polarity (in benzene derivatives—authors' note) found its due explanation only in Lowry's formula, but without the concept of contact bonds, this formula could not be proved and therefore it did not receive recognition" [24]. Since Chelintsev himself admits that the "contact bond" is only a "new name" [25] for the electrovalent bond, then the difference between the standpoints of Lowry and Chelintsev resides solely in the fact that, according to Chelintsev, the electrovalent (contact) bond may still be homeopolar.


(I)

(II)

The untenability of the concept of the homeopolar electrovalent bond was repeatedly and convincingly demonstrated at the Conference on the Theory of Chemical Structure. We shall not repeat all the statements, but we find it necessary to expose the sophism of those arguments with which Chelintsev seeks to defend the concept of the homeopolar electrovalent bond. This is all the more necessary since he takes the liberty, in a most unceremonious manner, of attributing to A. M. Butlerov (and not for the first time [26]) his own point of view—which is far removed from Butlerov's point of view.

G. V. Chelintsev "proves" the existence of the homeopolar electrovalent bond by the existence of special "supermechanical relations" between nuclei and electrons, and the well-known (in physics) electric and magnetic interaction between them is designated by a stroke of the pen as a "space-force", mechanical interaction. Of course such a hypothesis of the mechanical character of the electromagnetic interaction between atoms and molecules or between nuclei and electrons is quite untenable (it is, strictly speaking, a mechanical formulation of the problem); likewise there is no justification for the postulation by Chelintsev of certain "supermechanical relations" between nuclei and electrons, this being contradicted by all the existing evidence for physical—according to Chelintsev's definition "mechanical"—relations between them.

We agree with A. N. Nesmeyanov who, in reply to Chelintsev, writes: "A molecule is, of course a nuclear-electronic formation built up in a definite manner, and no special forces enter into its construction, apart from the nuclear-electronic interaction known to physics...the essential feature of a reaction, the essential feature of chemical dynamics consists in the fact that a reaction of one set of chemical substances gives rise to another set of substances, and this essential feature must not be ignored for it constitutes the specific objective of chemical science. However, this essential feature of a higher (compared with the physical and mechanical) form of movement does not require any special mechanism beyond the known interactions of nuclei and electrons" [27]. The subsidiary purpose of the concept of the "supermechanical"

relations between nuclei and electrons—namely, to lend a helping hand to the physically untenable and fundamentally superfluous hypothesis of the homeopolar electrovalent bond—is perfectly obvious. G. V. Chelintsev writes plainly: "The submitted proof* of the concept of the homeopolar electrovalent bond is governed by the concept of the supermechanical effect inherent in a system of electrons and nuclei" [28].

However, if we ignore the foregoing "proof", which Chelintsev had to base on the resonance-mesomeric creed, then there are no physical proofs whatsoever of the existence of those very "supermechanical" relations between nuclei and electrons (physicists must still only "concern themselves with this matter", asserts the author of the "new structural theory" [29]). Chelintsev thus takes refuge in historical arguments, attempting to rely on the authority of the Butlerov theory of chemical structure. He placed the sign of equality between his above-quoted concept and the views of Butlerov, from which it follows that the historical advances of Butlerov's theory are a confirmation of the "supermechanical" concept of Chelintsev: "This concept"—the statement continues [28]—"corresponds to the Butlerov concept of chemical structure...Since, as demonstrated by the historical development of organic chemistry, only Butlerov's affirmation of the validity of the formulas of chemical structure leads to an understanding of the laws of chemical phenomena and to their practical exploitation, it is obvious that the concept of the supermechanical relations between electrons and nuclei corresponds to reality". Is it really obvious?

Chelintsev argues that Butlerov put aside "the consideration of the spatial arrangement of atoms", but in addition—and this the author of the "new structural theory" passes over in silence—Butlerov put aside the problem of the nature of the relations of atoms in a molecule, in other words the problem of the nature of the chemical bond, i.e. the very subject on which Chelintsev comments. This is clear from the same passage which Chelintsev himself quotes [30]: "We are fully entitled"—wrote Butlerov—"to speak of the mutual chemical relation of atoms in a molecule as if it were a real relation. Putting aside the question of the nature of this relation (our italics - author's note) and the whole of the spatial concepts, we arbitrarily assign to it the name of "link" or "bond". As for the rest, in those rare passages where Butlerov touches on the nature of the interatomic bond, he speaks of interference of movement (e.g. vibration) of one atom by the movement of another atom [32]. In addition, as already noted above, Butlerov put to one side the question of the spatial relations of atoms only temporarily, "in the meantime", a fact that must have been known to Chelintsev. Consequently, the claim of Chelintsev that his concept of the "supermechanical" relations of electrons and nuclei (conflicting with all other ideas about physical interaction) "corresponds to the Butlerov hypothesis of chemical structure" is nothing less than a stain on the reputation of the great Russian chemist—A. M. Butlerov.

Sometimes these dubious "proofs" of G. V. Chelintsev are directly due to that obvious "ignorance of the history of the development of the problem of structure" of which he lightly accuses others and which leads him so far as to deny Butlerov's priority in the creation of the theory of chemical structure. As we know, foreign and some Russian historians have frequently reiterated that structural formulas were already being used by chemists at the end of the fifties of the past century, i.e. chemical structural formulas. This is the chief link in the version first composed by Kekulé and Lothar Meyer, according to which Kekulé was actually the author of the structural theory. Actually, however, even in 1863 (Kekulé was using the type formulas (first edition of the second volume of the textbook of organic chemistry) which, as he himself repeatedly emphasized, are only the formulas of transformation of substances. As V. V. Markovnikov has convincingly shown, even in 1864 Kekulé in his textbook still adhered to formulas of transformation and not of structure: "...the renunciation (of types – Authors' note) is only apparent. No types, but the meaning of the formulas remained as previously" [33]. In contrast to Kekulé's formulas, those of Couper indicated the linkage of atoms in the molecule, but they did not rest on experiment and were governed by the ability of the substances in question to enter into definite reactions. Couper was influenced in their derivation only by the formal rules of valency of elements and, evidently, in the majority of cases he still tended to produce symmetrical formulas. In comparison, therefore, with Butlerov's formulas, those of Couper are arbitrary pseudo-structural schemes.

* It follows, according to Chelintsev, from a comparison of the "new formula of benzene with the hexatriene formula of its pseudomer" that in the transition from the nonexistent "pseudomer" to real benzene an energy gain occurs. In what respect, then, does this "proof" differ from the "proof" of the theory of resonance, according to which a similar energy gain follows from a comparison of real benzene with the resonance form (i.e. the "pseudomer" of benzene), represented by the Kekulé hexatriene formula which Chelintsev has so often anathematized?

We thus see the profound error of the assertion of the existence of pre-Butlerov structural formulas which more satisfactorily expressed the chemical properties of substances. Furthermore, in the words of Chenlintsev, "structural formulas were written even before Butlerov", but they were regarded as convenient means of expression of the methods of preparation or of the chemical properties" [15] of the molecules. It is clear that these words are only applicable to the type formulas of Gerhardt, Kekulé and their successors. "The instrument which was to be judged the most important instrument in chemical science – writes Chelintsev later – was still very coarsely fashioned but was nevertheless available. However, methods were not known for its utilization. These methods were discovered by A. M. Butlerov" [15]. According to Chelintsev, therefore, Butlerov in his theoretical studies in the early sixties was already utilizing finished structural formulas. The same assertion was made in their time by Kekulé and Lothar Meyer, who did not hesitate to garble historical facts.

Lack of space limited the size of our article and we were unable to deal with other errors of G. V. Chelintsev (knowledge of "mutual influences" on the energy relations of atoms [30], the statement that one of the obstacles to the recognition of his benzene formula has "an ideological character" [28], etc); nor have we composed a final answer to a whole series of his "accusations" and malicious innuendoes, such as : "By the term 'modern chemists' B. A. Kazansky and G. V. Bykov imply only the supporters of the mesomer-resonance theory of Ingold and Pauling" [17].

We have no thought at all of denying the right of G. V. Chelintsev, as well as that of any Soviet scientist, to put forward hypotheses relating to any field of chemistry. We even think that some of our chemists avoid expressing their views on theoretical matters due to fear of criticism, especially when it is so crude and tendentious as that of G. V. Chelintsev, or due to diffidence about the results of discussions, or to disinclination, in general, to enter into polemics. In saying this, we are not reproaching Chelintsev. We willingly acknowledge his services in opposing by positive action the mesomer-resonance theory, the criticism of which by Chelintsev was of undoubted value. Nevertheless, it is impossible to ignore the scientific untenability of the hypothesis of Chelintsev, which he too hastily put forward as a theory. Moreover, its author (forgetting the words of Butlerov: "He who is filled with vain conviction of the truth of his scientific theory is virtually reverting from science to a dogmatic creed" [34] suggests that "other formulas of the chemical structure of conjugated compounds than the formulas of the new structural theory can exist within the framework of modern electron-nuclear concepts" [35]. Consequently, who dares to criticize the new structural theory! How should there be a battle of ideas between other chemists and the author! And any publication opposing his "theory" is made to appear a reprehensible heresy. Anybody writing in opposition to Chelintsev's theory or ignoring it is readily accused by him of "mechanism", "agnosticism", "machism", and similar "isms". Chelintsev prosecutes the campaign for his theory with a vociferous and defamatory slogan: He who is against me is against dialectical materialism. Under the guise of the fight for the dialectic-materialistic development of the Butlerov doctrine of chemical structure, G. V. Chelintsev is at present engaged in defaming existing and potential opponents of his "theory", resorting to methods which cannot fail to shame Soviet chemistry.

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ELEMENT ANALOGS OF THE PERIODIC SYSTEM

E. P. Ozhigov

In composing his ingenious periodic system, D. I. Mendeleev proceeded from the harmony between the physico-chemical properties of the elements and their masses.

Forced to use only one quantitative characteristic of the element – its atomic weight, D. I. Mendeleev established an interrelationship between the atomic weights and the chemical properties of the elements, and developed the theory for correlation of atomic weights, which was subsequently the object of attention by investigators for 50-60 years of the last century (Dumas, Pettenkofer, L. Meyer, and others).

At the present time these concepts of D. I. Mendeleev have acquired considerable interest in regard to investigation of the periodic properties of the atomic nucleus.

D. I. Mendeleev remarks that "those elements which are similar in chemical properties are either close together in atomic weights (such as Pt, Ir, Os), or increase uniformly and consecutively (such as K, Rb, Cs). Values for the atomic weights of elements belonging to the neighboring long periods differ by approximately 45, for example, K–Rb, Cr–Mo, Br–I. However, elements of a given series possess smaller differences in atomic weights. The differences between the atomic weights of Li, Na and K are the same, approximately 16, for Ca, Mg and Ba the same, for Si–C equal to 16.1, for S–O equal to 16.06 and for Cl–F equal to 16.45. As the atomic weights increase, the elements of one group from two adjacent short periods usually possess large differences (equal to about 20 Ti–Si = V–P = Cr–S = Nb–As, and so forth). For the heaviest elements the greatest magnitudes are reached, for example, 26 = Th–Pb, 26 = Bi–Ta, 25 = Ba–Cd, and so forth. Thus, though not clearly, even with the values of atomic weight for analogs, there is observed a relationship with change in properties [1]."

For the end of the periodic system, D. I. Mendeleev adopts a difference value of 90 between atomic weights of analogous elements (elements of the sixth and seventh periods).

Later, Aston [2] attempted to relate periodic properties of the atomic nuclei with the chemical properties of the corresponding elements. In his monograph he writes: "Examination of a table of mass numbers indicates that there are many instances where a difference of 44 in mass numbers is related to a difference of 18 for atomic numbers. These differences are related to atoms of analogous chemical properties such as Cl^{35}, Br^{79}. Likewise, in a long period a difference of 88 is related to a corresponding difference of 32, for example, Nb^{93}, Ta^{181}". Aston considers these correlations to be purely accidental.

Upon analyzing continuous series of natural isotopes, the authors have come to the conclusion that Mendeleev's values for atomic weight differences of the analogs (applicable to isotopes) reflect nuclear periodicity and represent junction points in the system which relate periodic properties of the atomic nuclei with periodicity in their electronic structures.

The author has established that in the short periods (the second and third) the characteristic difference between the mass numbers for a series of 8, is 16 for a difference of 8 between the atomic numbers, and a difference of 44-48 between mass numbers for a difference of 18 between the atomic numbers of 18 (the medium-length periods), while the characteristic difference in mass numbers is 88-90 for the difference of 32 between the atomic numbers in the long periods. This allows placement of an isotopic series for one period under another period, thus to obtain an isotopic system externally resembling the D. I. Mendeleev's system of elements. The periodicity of elements with even and with odd numbers is shown by an upward displacement for element isotopes with odd numbers, which are quite well reflected in the rules of Shchukarev-Mattaykh, Aston and others.

TABLE 1

No.	Periods compared	Differences between periods (in rounded-off units of atomic weight)	
		For the analogous elements, according to Mendeleev	According to the tables for principal isotopes of elements
1	2nd and 3rd	16	16
2	4th and 5th	45	44-48
3	6th and 7th (following the lanthanoids)	90	88-90

For example, from an analysis of a series of isotopes of the second and third periods it can be seen that the pleiads can be arranged under one another in regular fashion, and at the same time those isotopes with similar nuclear structures will possess adjacent values of nuclear spin (Li^7 and Na^{23}, B^{11} and Al^{27}, N^{15} and P^{31}, O^{16} and S^{32}, F^{19} and Cl^{35}). At the same time there also appears a periodic repetition in the chemical properties of the elements; the analog difference of 16 falls within the range indicated by D. I. Mendeleev.

Along with this there are isotopes where the difference of 16 in the atomic numbers is not related to the repetition of chemical properties($B^{10}-Mg^{26}$, $N^{14}-Si^{30}$, $Ne^{21}-Cl^{37}$); however these exceptions do not violate the general rule, since there cannot exist a perfect mathematical coincidence in difference because of greater increase in number of nuclear neutrons as compared with the number of protons.

It is of interest to mention that the isotopes of greatest life span, among the artificial and the naturally-radioactive elements, correspond to the above-indicated differences. Thus, under isotope Mn^{55} is placed the complete analog – isotope Tc^{99} (a difference of 18 in atomicnumbers and a difference of 44 in mass numbers), which possesses a half-life period of $4 \cdot 10^6$ years.

The difference values in atomic weights for the analog elements coincides closely with the difference values for the mass numbers of the principal isotopes of the same elements (Table 1).

TABLE 2

Symbols of elements, and their atomic weights	Th–Ce 232.12-140.13	Pa–Pr 231-140.92	U–Nd 238.07-144.27	Np–Pm 237-147	Pu–Sm 239-150.43	Am–Eu 241-152	Cm–Gd 242-156.
Difference value. . .	91.99	90.08	93.80	90	88.57	89	85.1

Contemporary science does not give an explanation for this phenomenon, but apparently its basis lies in a periodic construction of the nuclei from specific structural units.

According to modern theoretical concepts [8,9], protons and neutrons form completed layers in the nuclei, which also determine nuclear periodicity.

A revelation of the role and the significance of D. I. Mendeleev's difference values in atomic weights of element analogs is not only of historical interest, but also possesses considerable significance for elucidation of the problem of methods for development of the periodic system. Inasmuch as the difference value for atomic weights of element analogs fluctuates around a certain average value, and is close to the difference between the mass numbers of their principal isotopes, it might be possible from this average to find the probable mass numbers for the principal isotopes of the new elements which have not as yet been discovered.

As is known, the question of possible new isotopes for elements 96, 97 and 98 is now being debated in the literature.

By making use of the concepts concerning the difference values of atomic weights between elements of the actinide and of the lanthanide groups, this problem might be approximately solved. Atomic weights for the principal isotopes of the transuranium elements have been taken from tables published recently [3].

It can be seen from Table 2 that there exists an abnormally low difference value in atomic weights for the pair, Cm–Gd, indicating that the Cm isotope with mass number 242 is not the principal one.

TABLE 3

Element No. 97

Isotope mass	240	241	242	243	244	245	246	247	248	249	250
Type of radioactive decomposition . .	K	K	K	K	K	α	α	α	—	—	—
Half-life period . .	Min.	Min.	Min.	Hours	Hours	Days	Years	Years	Years	Years	Years

Element No. 98

Isotope mass	243	244	245	246	247	248	249	250	251
Type of radioactive decomposition.	K	α	K	α	α	α	α	—	—
Half-life period	Min.	Min.	Days	Hours Days	Years	Years	Years	Years	Years

Mass numbers for the principal isotopes of Cm might be determined by systematic addition of the difference 88, and of the difference 90.45 (the average arithmetic value from the element differences preceding Cm) to the atomic weight of Cm.

The resulting numbers 244.90 and 247.35 define not the average atomic weight (average atomic weights for the transuranium elements possess no meaning), but rather the order and the numerical values for the most stable isotopes, including the Cm pleiad. Apparently the mass numbers 243, 244, 245, 246, 247, 248 and 249 should definitely be included in these series. Among the elements of even numbers, more probable is the presence of isotopes of even mass numbers possessing greater half-life periods; therefore, the most stable isotopes should be associated with isotopes of mass numbers 246 and 248. The series presented coincides fundamentally with the series predicted by Seaborg [4].

Similarly, with element 97 the most stable isotopes, with masses 247 and 249, result from adding the differences 88 and 90 to the atomic weight of Tb = 159.2. The principal isotopes for element 98 could be obtained by adding 88 and 90 to the atomic weight of Dy which is equal to 162.46. In such a case, the principal isotopes for element 98 would be 250, 251 and 252. These data for the principal isotopes of the elements Bk and Cf are in satisfactory agreement with the data of A. P. Znoiko [5] and of I. Selinov [6], resulting from other theoretical concepts. We shall present a theoretical series of isotopes for the elements according to A. P. Znoiko [5].

I. Selinov [6] continues the isotopic series for element 98 with mass numbers. 252 $|\alpha|$ 253 $|\beta^-|$ 254 $|\alpha|$ 255 $|\beta^-|$ 256 $|\beta^-|$.

It can be seen from Table 3 that the Mendeleev atomic weight differences for the element analogs have not lost their significance up to the present day.

Taking into account D. I. Mendeleev's observations concerning element pairs (discussed in the works of S. A. Shchukarev [7]), and the fact that difference values in the atomic weights of element analogs of the periodic system coincide with difference values in the mass numbers of isotope analogs, the conclusion might be drawn that to D. I. Mendeleev belongs the priority of having demonstrated, along with the chemical periodicity, a certain nuclear periodicity, the significance of which, in view of the status of science in his time, was not clear to him.

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IONIC RADII AND IONIZATION POTENTIALS

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The ionization potentials are known for a majority of the chemical elements. The existence of a tremendous amount of experimental material in this field has made it possible to work out generalizations and to derive a number of functional relationships between the ionization potential values and characteristics of the atoms. These functions in a majority of cases extend only to atoms with a minimum number of electrons. The validity of periodicity for the ionization potentials with increase in Mendeleev number has been established.

A great number of empirical and semi-empirical equations have been proposed [1] for calculating the ionization potentials of isoelectronic atoms and ions. Some authors, and in particular Wasastjerna [2], have established a relation between the ionization potential values and the distance between nucleus and electron. Undoubtedly there exists a relation between ionization potential and the radius of the ion formed in the ionization process.

An increase in nuclear charge (the Mendeleev number) should lead to an increase in the ionization potential; however, the radius increase formed in the ionization process should lead to the reverse effect. The empirical equation (1) proposed by the author reflects the reverse action of these two factors:

$$I = \frac{A \log Z + B}{r^{3/2}}. \quad (1)$$

In this equation I = ionization potential, r = radius of the ion formed (the author used Goldschmidt's ionic radii in all cases), Z = Mendeleev's number (atomic number), A and B = constants.

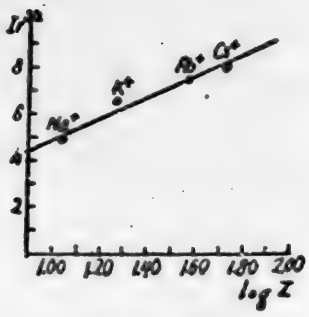

Fig. 1. Graph of the Ionization Potential Dependence Upon Atomic Number.

Equation (1) can be slightly modified:

$$Ir^{3/2} = A \log Z + B. \quad (2)$$

After such modification, the right side of the equation conforms completely to the expression for changes in thermochemical values as proposed by A. F. Kapustinsky [3].

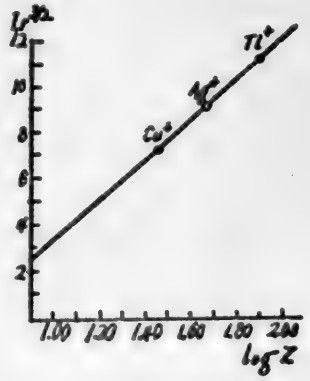

Fig. 2. Graph of Ionization Potential Dependence upon Atomic Number.

In the graphs given (Figs. 1,2,3 and 4) it has been demonstrated that the derivative $Ir^{3/2}$ is actually found to be a linear function of the atomic number. At the same time there appear two groups of ions which appear to differ sharply: a) ions with the inert gas structure (8-electron ions); and b) ions with d- and s-electrons (18-, 18 + 2-electron ions, and also incomplete electronic structures).

The A and B constants in Equation (1) were found with the aid of the graph given. Upon substitution of the numerical values for these constants into Equation (1), the following equations resulted:

$$I_1 = \frac{4.9 \log Z}{r^{3/2}}, \quad (3a)$$

$$I_1' = \frac{8.8 \log Z - 5.5}{r^{V_2}}, \tag{3b}$$

$$I_2 = \frac{14.6 \log Z}{r^{V_2}}, \tag{3c}$$

$$I_2' = \frac{33.3 \log Z - 29.0}{r^{V_2}} \tag{3d}$$

Equations (3a) and (3c) define, respectively, the ionization potentials for one and for two electrons in those cases where the basic structure is that of an inert gas. If the basic structure remaining after ionization has a different structure, then Equations (3b) and (3d) should be applied for calculation of the ionization potentials for the 1st and 2nd electrons.

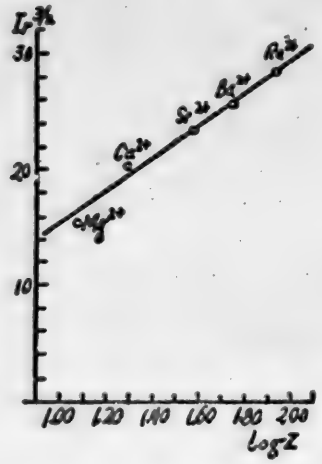

Fig. 3. Graph of Ionization Potential Dependence Upon Atomic Number.

The author has used Equations (3b) and (3d) to calculate ionic radii, since the data for ionization potentials are more extensive than data for ionic radii values. Calculation results are presented in Table 1. Primary data for the ionization potentials were taken from Lisitsin's abstract.

A majority of the ionic radii values given here have been calculated for the first time; however, some of them were reported earlier in the literature.

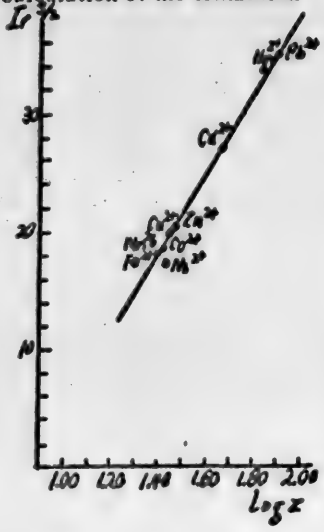

Fig. 4. Graph of Ionization Potential Dependence Upon Atomic Number.

B. F. Ormont [4] quotes values of 0.76 and 0.72 A, respectively, for the ionic radii values of Ti^{+2} and V^{+2}. These numbers almost coincide with the ones calculated by the author. The author's values with respect to Pd^{+2} and Cu^{+2} differ from the values quoted by B. F. Ormont. He gives values of 0.72 and 0.51 A for Pd^{+2} and Cu^{+2}. The author considers that the last two values differ from the actual values. The radius of the Pd^{+2} ion (0.72 A) is found to be smaller than the radius for the Ni^{+2} (0.78 A). Moreover, Pd is in the 5th period and Ni in the 4th; and, further, the ions for elements of the same group increase with an increase in atomic number. According to experimental data, the similarly-constructed NiF_2 and PdF_2 distances, M and F are respectively equal to 2.00 and 2.15 A, i.e., the radius of the Pd^{+2} ion is larger by 0.15 A than the Ni^{+2} radius, which is in approximate agreement with the author's data.

According to B. F. Ormont [4], the value for the ionic radius of Cu^{+2} differs sharply from the radii of doubly-charged ions for all elements of the 4th period sub-groups. The Cu–F distance in the CuF_2 lattice is 2.34 A [4], which likewise does not agree with Ormont's data.

By utilizing the entropy value for the Cu^{+2} ion in aqueous solution, A. F. Kapustinsky calculated the radius value for this ion [5]. It was found to be equal to 0.82 A; this value coincides well with the one calculated by the author.

The Sn^{+2} ionic radius value (1.17 A) differs somewhat from the value calculated by A. F. Kapustinsky [6]. This difference is explained by the fact that thermochemical calculation of the Sn^{+2} radius was carried out by the use of a first approximation equation for lattice energy (and further, A. F. Kapustinsky obtained a more accurate equation [7]), and in addition, in calculating the radius, the author proceeded from a hypothesis concerning the type of ionic relation in the compounds $SnCl_2$ and SnS. Meanwhile, the type of relation evidently differs from the ionic type, and the A. F. Kapustinsky equation gives somewhat lowered results.

The Ge^{+2} ionic radius value (0.98A) found by Powell and Brewer differs but little from the one calculated by the author.

To verify the ionic radii values obtained, the author, utilizing them, has calculated the lattice energies for tin, chromium, vanadium and indium. The required thermochemical data for compounds of the remaining elements are not available.

TABLE 1

Radii of Certain Ions, Calculated from the Ionization Potentials•

Ion	Atomic number	Total ionization potential (electron volts)	Radius (in Angstroms)	Ion	Atomic number	Total ionization potential (electron volts)	Radius (in Angstroms)
monovalent ions				divalent ions			
Ni^{+}	28	7.61	0.96	Cr^{+2}	24	23.3	0.81
Ga^{+}	31	5.97	1.17	Cu^{+2}	29	27.9	0.80
Pd^{+}	46	8.3	1.05	Ga^{+2}	31	26.4	0.85
In^{+}	49	5.76	1.38	Ge^{+2}	32	23.9	0.93
Pr^{+}	78	8.88	1.16	Pd^{+2}	46	28.2	0.96
divalent ions				Ag^{+2}	47	29.0	0.95
				In^{+2}	49	24.57	1.07
Ti^{+2}	22	20.4	0.77	Sn^{+2}	50	21.9	1.17
V^{+2}	23	~20.8	~0.73				

In the compounds investigated, the type of relation differs from the ionic: therefore, to calculate the lattice energy, the author used an equation developed earlier [9]:

$$U = U_i + 250[0.5 + 0.002(I_2 + 1/4\theta - 2E + D_{x_2} - U_i)]^2. \qquad (4)$$

where U = lattice energy; U_i = lattice energy calculated from the Kapustinsky equation; I_2 = ionization potential for two electrons; θ = characteristic temperature for the metal; E = electronic affinity of the x atom, and Dx_2 = dissociation energy of the x_2 molecule.

TABLE 2

Lattice Energies for Certain Salts

Compounds	Lattice energy		Compounds	Lattice energy	
	according to equation (kcal)	from experimental data (kcal)		according to equation (kcal)	from experimental data (kcal)
$SnCl_2$	545	538	$CrCl_2$	617	604
$SnBr_2$	630	637	CrI_2	585	584
SnI_2	516	515	VCl_2	600	589
$Sn(OH)_2$	630	637	$InCl_2$	562	578

The lattice energy value calculated from Equation (4) is given in Table 2. Data necessary for calculations were taken from sources [9] published earlier and from tables compiled by Britske and Kapustinsky [10].

The values calculated according to Equation (4) were compared with those calculated from experimental thermochemical data. There was observed in all cases a satisfactory conformity between calculated and experimental values.

• After dispatch of manuscript to press, the radius of the Francium ion (Fr^{+1}) was calculated by Finkelburg and Stern and was found to be equal to 1.78 Å.

Having now at one's disposal a considerable amount of data for the radii of mono- and of divalent ions, certain regularities can be detected in ionic radii modifications during change in atomic number (Mendeleev number). A compilation of the ionic radii is given in Table 3.

TABLE 3

Radii of Monovalent and Divalent Ions

Atomic number	Ion	Radius	Atomic number	Ion	Radius	Atomic number	Ion	Radius
5	Li^{+}	0.78	4	Be^{+2}	0.34	32	Ge^{+2}	0.93
11	Na^{+}	0.98	12	Mg^{+2}	0.78	38	Sr^{+2}	1.27
19	K^{+}	1.33	20	Ca^{+2}	1.06	46	Pd^{+2}	0.96
28	Ni^{+}	0.96	22	Ti^{+2}	0.[illegible]	47	Ag^{+2}	0.95
29	Cu^{+}	0.96	23	V^{+2}	0.73	48	Cd^{+2}	1.03
31	Ga^{+}	1.17	24	Cr^{+2}	0.81	49	In^{+2}	1.07
37	Rb^{+}	1.49	25	Mn^{+2}	0.91	50	Sn^{+2}	1.17
46	Pd^{+}	1.05	26	Fe^{+2}	0.83	56	Ba^{+2}	1.43
47	Ag^{+}	1.13	27	Co^{+2}	0.82	63	Eu^{+2}	1.25
49	In^{+}	1.38	28	Ni^{+2}	0.78	80	Hg^{+2}	1.12
55	Cs^{+}	1.65	29	Cu^{+2}	0.80	82	Pb^{+2}	1.32
78	Pt^{+}	1.16	30	Zn^{+2}	0.83	88	Ra^{+2}	1.52
81	Tl^{+}	1.49	31	Ga^{+2}	0.85			

As the atomic numbers of the elements change, the radii of identically charged ions change periodically. Upon transition from the basic 8-electron structures to the d-electron structures, contraction always occurs (K^{+}–Cu^{+}, Rb^{+}–Ag^{+}, Ca^{+2}–Ti^{+2}, Sr^{+2}–Pd^{+2}, etc.). Upon filling in the d-levels, an approximate stability for the ionic radii (Ti^{+2}–Zn^{+2}, Pd^{+2}–Cd^{+2} etc.) is maintained. With respect to this fact, the ionization potential constantly increases with increase in atomic number of the element. When the s-levels are filled in with electrons, a sharp increase in ionic volume is observed (Zn^{+2}–Ge^{+2}, Cd^{+2}–Sn^{+2}, Hg^{+2}–Pb^{+2}, Ag^{+}–In^{+} etc.), and in connection with this a certain decrease of the ionization potential.

For the groups of the periodic system, there is always observed an increase in ionic radius with increase in atomic number. The ionic radii increases slow down somewhat after the lanthanide groups (lanthanidal contraction). Connected with this circumstance are exceptionally high ionization potential values for a majority of the sixth period elements, and a high stability (18 + 2) for the electronic structure of this period (Tl^{+}, Pb^{+2}, Bi^{+3} etc.).

SUMMARY

1. An empirical equation establishing a relationship between the ionic radii and ionization potentials has been proposed.

2. Ionic radii have been calculated for 15 ions, the accuracy for some of the values of which have been verified by calculation of the lattice energies of the salts.

3. Common mechanisms for changes in the radii of identically-charged ions of the D. I. Mendeleev periodic system have been established.

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A PHYSICO-CHEMICAL INVESTIGATION OF THE SYSTEM $NH_4Br \cdot Al_3Br_9 - C_6H_5NO_2$ (ELECTROCONDUCTIVITY, VISCOSITY AND SPECIFIC GRAVITY)

I. S. Bigich and B. V. Sakhnovskaya

In the preceding works [1] it has been demonstrated upon calculation of viscosity in the region of high concentration, that the molecular electroconductivity for nitrobenzene solutions of aluminum bromide complex compounds assumes an abnormal character. The existing theories of abnormal molecular electroconductivity can be reduced to essentially two opposing theories. The first theory explains the abnormal course of the curves μ and φ on the grounds of disruption of the current-conducting complexes [2], and the second, being based upon the modern concept of liquid body structure, allows that in concentrated solutions there exists a definite order, characterized by the presence of structural groupings which possess internal conductivity. Upon dilution these groups diffuse to form ion pairs, as the result of which a fall in molecular electroconductivity [3] is observed.

According to the latter theory, an abnormal course of the μ-φ curve should appear for all concentrated solutions in calculation of viscosity. The authors considered it necessary to verify this statement by an investigation of the system $NH_4Br \cdot Al_3Br_9 - C_6H_5NO_2$. The composition of such a compound was established by thermal analysis [4].

Electroconductivity, viscosity and specific gravity measurements, and preparation of the $NH_4Br \cdot Al_3Br_9$ complex solutions were carried out in exactly the same manner as was described in the preceding articles [1]. Solutions of the required concentrations were prepared in quantities which permitted simultaneous measurements of electroconductivity, viscosity and specific gravity. Before dissolution, the complex was fused. Dissolution of $NH_4Br \cdot Al_3Br_9$ complex in nitrobenzene proceeded with heat evolution. The color of the solution changed from straw-yellow to red-brown with increase in concentration. During the experiments the vessel for measurement of electroconductivity, the viscosimeter and the pycnometer containing the solution to be investigated were placed in a water thermostat. The temperature in the thermostat fluctuated within the range of $\pm 0.05°$.

By investigations on the electroconductivity of the binary system $NH_4Br - AlBr_3$ in benzene [5], xylene [6], ethyl bromide [7] and nitrobenzene [8] it was established that the specific electroconductivities for the solutions increase with increase in concentration of ammonium bromide. Investigators explain the increase in specific electroconductivities for ternary systems as compared with binary systems upon the basis of current-conducting complex formation.

I. S. Bigich [1] investigated the electroconductivity of the $NH_4Br \cdot Al_2Br_6$ complexes in nitrobenzene, in the concentration range 5.01 to 60.25%, and temperature range of 20-50°. The investigation has shown that as the concentration of complex increases, the specific electroconductivity passes through a maximum and then decreases. The maximum for the curve corresponds to 25-30% of the complex. With increase in temperature, the electroconductivity increases, and the curve maximum shifts to the side of higher electrolyte concentration.

Results of measurements on specific electroconductivity, as investigated by the author for the system $NH_4Br \cdot Al_3Br_9$ in nitrobenzene, are graphically presented in Figure 1.

The specific electroconductivity for this system, as with the system $NH_4Br \cdot Al_2Br_6$ in nitrobenzene, passes through a maximum at 25-30% concentration with an increase in concentration of the complex $NH_4Br \cdot Al_3Br_9$. An increase in temperature shifts the maximum toward higher concentration.

The authors have calculated the electroconductivities for the same solutions, corrected for viscosity, and likewise for specific electroconductivities. The calculation was carried out according to the formula $\kappa' = \frac{\kappa \eta_s}{\eta_\theta}$, where κ = the corrected specific electroconductivity, κ', η_s and η_θ = specific electroconductivity, solution viscosity and nitrobenzene viscosity, respectively.

As can be seen from Figure 2, the maximum on the specific electroconductivity curves disappears when a correction for viscosity is introduced, and the curves themselves possess a convexity toward the abscissa axis.

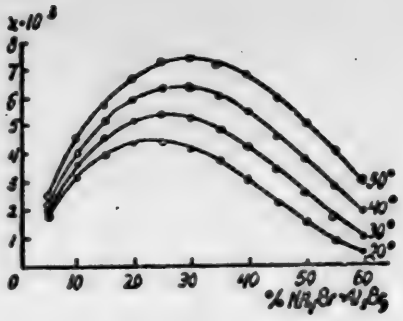

Figure 1. Specific electroconductivity of $NH_4Br \cdot Al_2Br_6$ solutions in nitrobenzene.

The curves of Figure 3 express the relation of molecular electroconductivity to dilution, as calculated for an electrolyte of the composition $NH_4Br-Al_2Br_6$.

As can be seen from Figure 3, the molecular electroconductivity curves also possess a normal character for aqueous solutions; the molecular electroconductivity values increase with increase in temperature. The molecular electroconductivity of the complex $NH_4Br \cdot Al_2Br_6$ in nitrobenzene is somewhat smaller than for the complex $NH_4Br \cdot Al_2Br_6$. With an increase in temperature, the molecular electroconductivity values increase, especially upon extensive dilution. Calculation of molecular electroconductivity, corrected for viscosity, was carried out according to the formula $\mu' = \frac{\mu \eta_s}{\eta_0}$ which is similar to the formula for calculation of corrected specific electroconductivity.

As can be seen from Figure 4, as the concentration of electrolyte increases, the molecular electroconductivity, corrected for viscosity, first decreases, passes through a maximum, and then increases gradually.

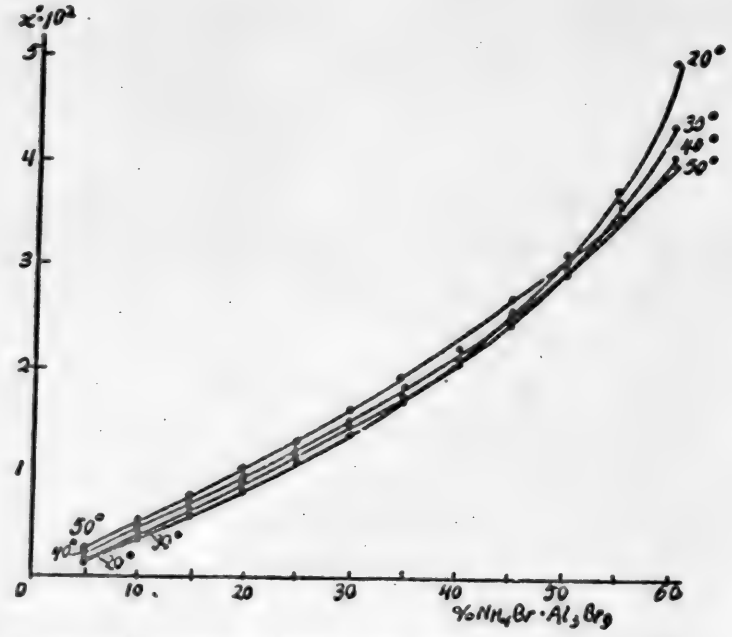

Figure 2. Corrected (for viscosity) specific electroconductivity of $NH_4Br \cdot Al_2Br_6$ solutions in nitrobenzene.

Such a course for the curves of corrected molecular electroconductivity of the solutions investigated indicates that an abnormal course for the $\mu'-(\varphi)$ curves appears in a solution with high dielectric constants upon introduction of a correction for viscosity.

Considering the fact that ammonium bromide does not dissolve in nitrobenzene in the absence of aluminum bromide, and that the dissolution process is related to complex formation, it should be expected, in accordance with the theory of current-conducting complexes, that the complex should be decomposed upon dilution, and that the insoluble component should precipitate out. However, this was not observed. Therefore, the authors consider that their experiments confirm the statement which E. Ya. Gorenbein [3] postulated concerning the nature of the concentrated solutions; any dissolved substance tends to transform into such a state as it might possess in the melted state, and at the same time the highest corrected molecular electroconductivity should correspond to the molecular electroconductivity for the individual electrolyte in the molten state.

In other words, an increase in the molecular electroconductivity, corrected for viscosity, as the electrolyte concentration is increased, depends upon the formation of structural groups which characterize the degree of their regular distribution in the solution. The maximum number of structural associations and also the greatest extent of order corresponds to pure electrolyte in the molten state. As dilution proceeds, there results a disintegration of the structural groups, which results in a decrease of the molecular electroconductivity, as corrected for viscosity. It is characteristic that the temperature effect upon corrected electroconductivity varies in accordance with concentration. In the low concentration range, electroconductivity increases with temperature increase, which is apparently explained by an increase in degree of dissociation, whereas in the high concentration range with temperature increase electroconductivity decreases, which is apparently related to a decreased extent of order for the electrolyte in the solution [3].

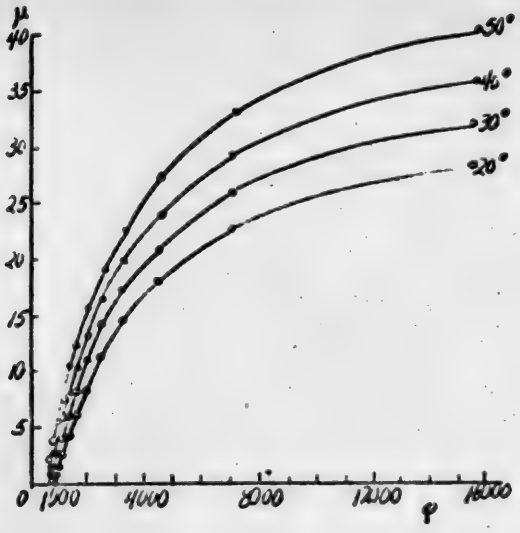

Figure 3. Molecular electroconductivity of $NH_4Br \cdot Al_2Br_6$ solutions in nitrobenzene.

The analogy between the electroconductivity curves of viscosity and of specific gravity for the $NH_4Br \cdot Al_2Br_6$ and $NH_4Br \cdot Al_2Br_6$ complexes which were studied in nitrobenzene gives basis for assuming that the molecular states of these substances in the solution are identical, and that the associations formed are likewise similar. Hence it follows that the mechanism of electric current passage in electrolytes is also identical.

Specific gravity of the $NH_4Br \cdot Al_2Br_6$ complex in nitrobenzene. This was determined under the same conditions as for electroconductivity. The specific gravity was measured by a pycnometer with tightly-ground stopper, on the neck of which were marked divisions to 0.01 ml.

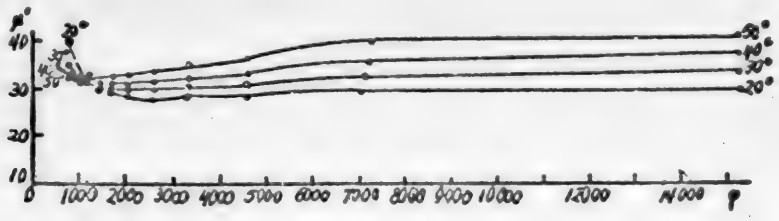

Figure 4. Corrected molecular electroconductivity of $NH_4Br \cdot Al_2Br_6$ solution in nitrobenzene.

As can be seen from Figure 5, the specific gravity for the system increases with an increase in complex concentration. A temperature increase leads to specific gravity decrease, which changes linearly. The d(c) curves possess convexity toward the abscissa axis.

Viscosity. Viscosity measurements for a solution investigated at the same concentration and temperature were carried out in an Ostwald viscosimeter, described in the works of I. A. Katsnelson and A. B. Bernstein [9].

As can be seen from Figure 6, values of solution viscosity for complex concentrations ranging from 5 to 45 % increase slightly at first and the curve slopes, and with further increase in complex concentration the slope of the curve increases sharply.

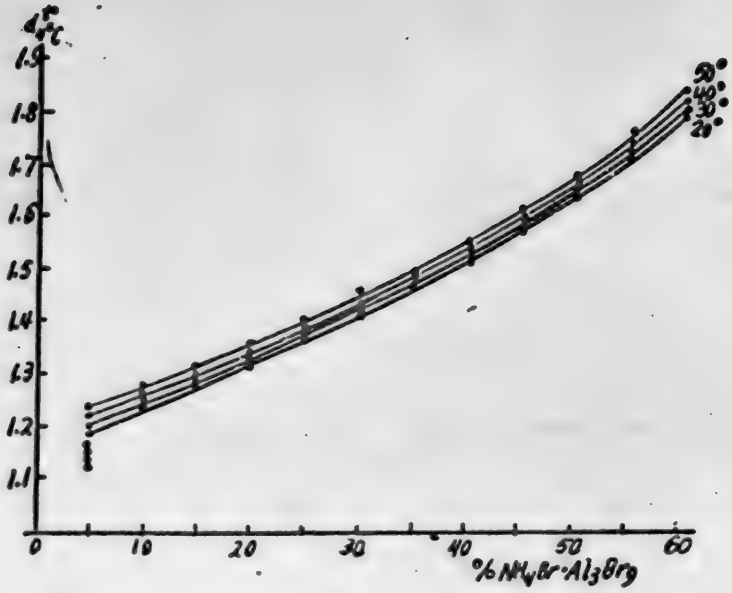

Figure 5. Specific gravity of $NH_4Br \cdot Al_3Br_9$ solutions in nitrobenzene.

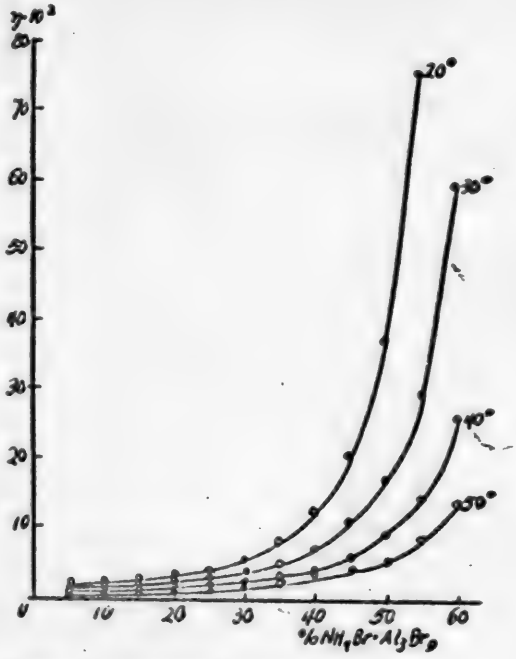

Figure 6. Viscosity of $NH_4Br \cdot Al_3Br_9$ solutions in nitrobenzene.

SUMMARY

1. The electroconductivity, viscosity and specif gravity for $NH_4Br \cdot Al_3Br_9$ complex in nitrobenzene, for th concentration range 5.00 to 60.09%, has been investigated at temperatures of 20, 30, 40 and 50°.

2. The specific electroconductivity curves pass through a maximum, and the molecular electroconductivity values increase with dilution.

3. When corrected for viscosity, the maximum o the specific electroconductivity curves disappears, and the molecular electroconductivity develops an abnormal character. Such a course for the curves confirms the state ment postulated by E. Ya. Gorenbein concerning the natur of concentrated solutions.

4. The similarity in the course of the curves for electroconductivity, viscosity and specific gravity for the $NH_4Br \cdot Al_3Br_9$ complexes investigated and for $NH_4 \cdot Al_2Br_6$ [1] in nitrobenzene, indicates that the nature of these systems is probably identical and that the associations formed are similar.

5. The specific and molecular electroconductiv ties increase with increase in temperature, while the viscosity decreases.

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REFRACTOMETRIC INVESTIGATIONS

I. REFRACTIVE INDEX ISOTHERMS FOR IDEAL SYSTEMS

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The present article is devoted to the problem of the relation of refractive index to the composition of an ideal system. It is usually assumed that for systems which are composed of non-interacting and non-associated components, and which satisfy the thermodynamic conditions for ideality, the refractive index will be found to be a linear function of the composition. However, up to the present time there has been no single viewpoint on which manner of expressing the composition might be considered to give additive refractive indices for ideal systems.

In the first article, which was devoted to refractometry as a method of physico-chemical analysis [1], the additivity of refractive index for ideal systems was utilized as a function of composition expressed in molar units:

$$n_{add} = n_1N_1 + n_2N_2 \qquad (1)$$

(n_1 and n_2 = the refractive indexes and N_1 and N_2 = the molar units of first and second components, respectively).

This position was substantiated by experimental data for the system, bromoform-chloroform, and for mixtures of "isofluid" liquids (isomeric xylenes, esters and others) which were investigated by O. M. Morguleva [2]. Assumption (1) is accepted by most authoritative manuals [3,4], and in a majority of the works on the refractometric physico-chemical method of analysis [5,6,7,8]. However, some authors [9,10,11] consider the refractive index for ideal systems to be a linear function of composition by weight (P) and not by molecular units:

$$n_{add} = n_1P_1 + n_2P_2. \qquad (2)$$

Assumption (2) apparently eliminates (1), but nevertheless the same investigators at times utilize in different articles correlation (1) [6,7,8] and correlation (2) [10,11], without reason for their selection.

Back in 1933 MacFarlane and Wright [12] indicated that, proceeding from the physical nature of the light refraction phenomenon, the refractive index of a mixture should be considered a function of composition in volumetric units (V). Using examples from several systems (hydrocarbons and their halogen derivatives) they demonstrated that the correlation

$$n_{add} = n_1V_1 + n_2V_2 \qquad (3)$$

is better fulfilled than (1) and (2). However, the results of this work in physico-chemical analysis were completely ignored. In 1940, M. Usanovich and A. Stepanyants [13] again indicated that the additive rule for refractive indices should be formulated in accordance with correlation (3), and not by (1), but again these recommendations in subsequent articles on refractometry were not given attention, perhaps due to the inadequacy of the work (the authors quoted data for only two systems selected at random). •

An explanation of refractive index isotherms for ideal systems is of major importance for the refractometric method of physico-chemical analysis. Unusual points and extremes in refractive index isotherms rarely occur, and the interaction of components for binary and ternary systems can be evaluated by the sign and magnitude of deviations from additivity, Δn:

$$\Delta n = n_{exp.} - n_{add} \qquad (4)$$

It is quite evident that the value and the sign for Δn depend not only upon the nature of the investigated system, but also upon selection of correlation (1), (2) or (3), for the calculation of $n_{add.}$ ••

• After the manuscript for the present article had been sent to press, Professor N. A. Trifonov (Kazan) brought to the attention of this author the fact that he and his students had independently come to a conclusion concerning additivity, $n_D(V)$ – see footnote to article in J. Phys. Chem. 21, 503 (1947).

•• Δn values, calculated according to (4), will be designated $\Delta n(N)$, $\Delta n(P)$ and $\Delta n(V)$, respectively, according to the different assumptions (1), (2) and (3).

The brief review of literature, as given above, indicates that this problem has not been given due consideration.

The experimental procedure for solving the problem in question consists of an investigation of mixtures of non-interacting and non-associating components A and B which differ considerably not only in refractive indexes, but also in densities (d), molecular weights (M) and molar volumes, i.e., corresponding to the conditions:

$$n_A \gg n_B \text{ or } n_A \ll n_B; \quad (5)$$

$$M_A \gg M_B \text{ or } M_A \ll M_B; \quad (6)$$

$$d_A \gg d_B \text{ or } d_A \ll d_B; \quad (7)$$

$$\frac{M_A}{d_A} \gg \frac{M_B}{d_B} \text{ or } \frac{M_A}{d_A} \ll \frac{M_B}{d_B}. \quad (8)$$

Maintenance of these conditions was found to be essential, since it is not otherwise possible to make a well-defined selection between concentration expressions in molar, weight or volume units (%). In addition to the above-indicated conditions, it should be borne in mind that in order to avoid unfounded conclusions due to random selection of systems, all cases of correlation in numerical values for component properties should be investigated. With the three usual methods of expressing concentration in weight (P), volumetric (V) and molar (N) units, the following six correlations are possible:

I. $P_1 > V_1 > N_1 \left(\text{at } M_1 > M_2,\ d_1 > d_2,\ \frac{M_1}{d_1} > \frac{M_2}{d_2}\right)$;

II. $P_1 > N_1 > V_1 \left(\text{at } M_1 > M_2,\ d_1 > d_2,\ \frac{M_1}{d_1} < \frac{M_2}{d_2}\right)$;

III. $V_1 > P_1 > N_1 \left(\text{at } M_1 > M_2,\ d_1 < d_2\right)$;

IV. $N_1 > P_1 > V_1 \left(\text{at } M_1 < M_2,\ d_1 > d_2\right)$;

V. $V_1 > N_1 > P_1 \left(\text{at } M_1 < M_2,\ d_1 < d_2,\ \frac{M_1}{d_1} > \frac{M_2}{d_2}\right)$;

VI. $N_1 > V_1 > P_1 \left(\text{at } M_1 < M_2,\ d_1 < d_2,\ \frac{M_1}{d_1} < \frac{M_2}{d_2}\right)$.

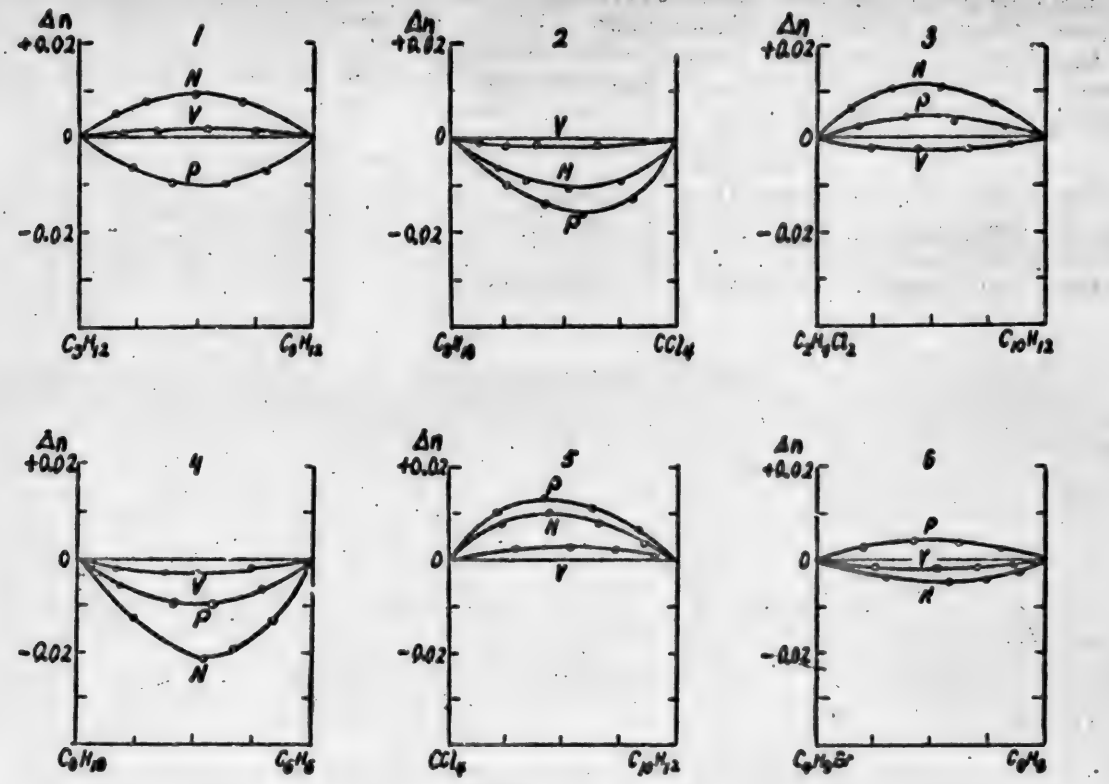
For calculation of Δn in physico-chemical analysis, this method should be used only for expression of compositions where Δn values are determined by the behavior of the components in the mixture, but not by the correlation of their physical properties. For selecting a method of expressing the composition, it is necessary, consequently, to develop the dependence of Δn upon the correlations I-VI. Having available the experimental data for all possible cases [I-VI for conditions (5-6)], a substantiated selection can be made between assumptions (1), (2) and (3).

The author has investigated refractive index isotherms for hydrocarbons and their halogen derivative mixtures which conform to conditions (5-8). The following systems were investigated for all possible combinations of components:

mesitylene – n-pentane (Case I);
carbon tetrachloride – 2,2,4-trimethylpentane (Case II);
bromobenzene – 2,2,4-trimethylpentane (Case II);
tetralin – dichloroethane (Case III);
benzene – 2,2,4-trimethylpentane (Case IV);
tetralin – carbon tetrachloride (Case V);
benzene – n-butyl bromide (Case VI).

The resulting data are presented in Figures 1-7, in the form of curves representing deviations from Δn additivity for various methods of expressing composition. The numbering for systems of the first six figures corresponds to correlations (I-VI), and the component of higher n_D^{20} is considered to be first.

As can be seen from the figures, the smallest deviations in additivity are observed in all cases where concentration is expressed in volume units. The $\Delta n(V)$ values for the systems examined do not exceed 0.003, while the $\Delta n(P)$ and $\Delta n(N)$ deviations reach 0.02-0.03, and at the same time it is quite obvious that the value and sign of $\Delta n(P)$ and of $\Delta n(N)$ are definitely dependent upon inequalities I-VI, and consequently are determined not only by their behavior in the mixtures, but also by the correlation of densities and molar volumes for the



Figures 1-6. Deviations in refractive indexes from additivity in relation to various methods for expressing concentration.

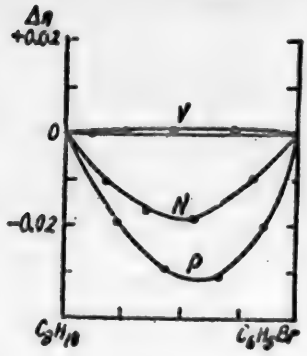


Figure 7. Deviations in refractive indexes from additivity for the bromobenzene-224-trimethylpentane system.

components. The values Δn(P) are positive for the 3, 5 and 6 systems when $d_1 \ll d_2$, and negative at $d_1 \gg d_2$.

In the 1,3 and 5 systems, where $\frac{M_1}{d_1} \gg \frac{M_2}{d_2}$, Δn(N) are positive, and in the 2,4 and 6 systems with $\frac{M_1}{d_1} \ll \frac{M_2}{d_2}$, Δn(N) values are negative. Deviations from additivity, Δn(V), in contrast to Δn(N) and Δn(P) are not connected with correlations I-VI, but are dependent upon system deviations from strict ideality, which show up in volume change upon mixing. The lack of dependence of Δn(V) upon correlations I-VI is illustrated by comparison of all figures given, and is shown with particular clarity in Figure 2 and Figure 7. Data are presented in these two Figures for mixtures of carbon tetrachloride and bromobenzene with 2,2,4-trimethylpentane. Both systems represent Case II of correlations in component properties. In accord with these facts, curves Δn(N) and Δn(P) are very similarly laid out; however, curve Δn(V) in the first system is negative, and in the second, positive.

As can be seen from Table 1, the sign of Δn(V) is determined by the sign of the volume change: if contraction is observed in the system then $\Delta n(V) > 0$; however, if expansion takes place $\Delta n(V) < 0$. The author found no exceptions to this rule for non-interacting and non-associating components, either in his own investigations, or upon searching the literature data.

From Table 1 and from what has been stated above, it follows that, generally speaking, the symbols Δn(N) and Δn(P) are not related to volume change. Attempts to assert this relationship [14] should be considered incorrect.

It should not be thought, however, that deviations from additivity $\Delta n(V)$ are caused exclusively by volum changes in the system. Correlation between $\Delta n(V)$ and volume changes actually take place in an overwhelming majority of cases for systems with association and interaction of the components. The author was able, however, to find two examples of systems with associated components where such relation does not exist. With mixtures of toluene and n-propyl alcohol [14], the contraction is accompanied by negative $\Delta n(V)$ values, and with the system isobutyl alcohol – methyl alcohol [15] the values $\Delta n(V)$ are positive with expansion.

From all that has been stated above, it follows that assumptions of rectalinearity of n isotherms as functio of molar and of weight units are for the most part inaccurate. It is more accurate to consider that the refractive index for ideal systems is a linear function of the volume units for the components. It should be mentioned that this statement is in conformity with the known fact of additivity of molecular refractions, and, in particular, is equivalent to the statement of molecular or specific refraction for ideal systems according to Gladstone-Dahl.

Additivity of specific refraction, according to Gladstone-Dahl, is expressed by the equation:

$$\frac{n-1}{d} = \frac{n_1-1}{d_1} P_1 + \frac{n_2-1}{d_2} \cdot P_2. \qquad (9)$$

Hence:

$$n = n_1\frac{d}{d_1} P_1 + n_2\frac{d}{d_2} P_2 + 1 - \frac{d}{d_1} P_1 - \frac{d}{d_2} P_2$$

But in ideal systems whose components are mixed without change in volume,

$$\frac{d}{d_1} P_1 = V_1, \frac{d}{d_2} P_2 = V_2 \text{ and } V_1 + V_2 = 1.$$

Consequently,

$$n = n_1V_1 + n_2V_2 \qquad (10)$$

TABLE 1

Volume Changes Upon Mixing, and the Signs $\Delta n(V)$, $\Delta n(N)$ and $\Delta n(P)$

System	Correlation of component properties	Volume change	Signs		
			$\Delta n(V)$	$\Delta n(N)$	$\Delta n(P)$
Mesitylene – n-pentane	I	–	+	+	–
Carbon tetrachloride – 2,2,4-trimethylpentane	II	+	–	–	–
Bromobenzene – 2,2,4-trimethylpentane	II	–	+	–	–
Tetralin – dichloroethane	III	+	–	+	+
Benzene – 2,2,4-trimethylpentane	IV	+	–	–	–
Tetralin – carbon tetrachloride	V	–	+	+	+
Benzene – n-butyl bromide	VI	+	–	–	+

Although it corresponds to experimental data for liquid mixtures somewhat better than other refraction formulas, the empirical formula of Gladstone-Dahl does not appear to be a strict and universal expression of the relation between refractive index and the density of the substance. Hence it follows that the assertion of n(V) additivity for ideal systems in like manner cannot be considered rigorously correct. The form of the isotherms for n(V) systems which satisfy the thermodynamic requirements for ideality can evidently vary somewhat, depending upon the optical properties of the component molecules which determine accurate expression of the refraction formulas for such components.

The problem of importance of refractometric data and, in particular, the $\Delta n(V)$ values, for purposes of physico-chemical analysis, requires further study. In any event, the numerous attempts to relate deviations from additivity $\Delta n(N)$ and $\Delta n(P)$, as being due solely to the interaction or dissociation of components possessing different molecular volumes and densities, should be considered erroneous in the main. Deductions of old works which were based upon such interpretations of $\Delta n(N)$ and $\Delta n(P)$ values, lack sufficient argumentive strength and are in need of revision.

EXPERIMENTAL

For each pair of components 4 mixtures were investigated with concentrations of about 20, 40, 60 and 80%

TABLE 2

Experimental Data for the Refractive Indexes and Densities of the Systems Investigated

P_1	V_1	N_1	n_D^{25}	d_4^{25}	$\Delta n(P) \cdot 10^4$	$\Delta n(V) \cdot 10^4$	$\Delta n(N) \cdot 10^4$
			Mesitylene – n-pentane				
0	0	0	1.3574	0.6259	–	–	–
0.2270	0.1751	0.1478	1.3835	0.6702	−61	+ 12	+ 51
0.3960	0.3216	0.2790	1.4045	0.7074	−91	+ 14	+ 75
0.6222	0.5435	0.4930	1.4364	0.7618	−94	+ 18	+ 90
0.7973	0.7398	0.6990	1.4638	0.8078	−68	+ 13	+ 71
1	1	1	1.4994	0.8658	–	–	–
			Carbon tetrachloride – 2,2,4-trimethylpentane				
0	0	0	1.3915	0.6918	–	–	–
0.2581	0.1312	0.2053	1.3999	0.8090	− 94	− 6	− 58
0.4252	0.2431	0.3545	1.4073	0.9092	−135	−10	− 86
0.5909	0.3854	0.5175	1.4170	1.0368	−153	−11	−102
0.8082	0.6465	0.7578	1.4350	1.2728	−123	−11	− 88
1	1	1	1.4605	1.5937	–	–	–
			Bromobenzene – 2,2,4-trimethylpentane				
0	0	0	1.3915	0.6918	–	–	–
0.2385	0.1263	0.1856	1.4127	0.7948	−190	± 0	−100
0.4383	0.2635	0.3620	1.4364	0.9080	−289	+ 5	−160
0.6584	0.4710	0.5837	1.4717	1.0750	−307	+ 9	−180
0.8505	0.7245	0.8054	1.5144	1.2792	−202	+10	− 95
1	1	1	1.5598	1.4970	–	–	–
			Tetralin – dichloroethane				
0	0	0	1.4448	1.2522	–	–	–
0.1887	0.2306	0.1482	1.4660	1.1848	+ 27	−14	+ 66
0.3944	0.4562	0.3277	1.4875	1.1205	+ 41	−19	+106
0.6066	0.6652	0.5358	1.5081	1.0622	+ 40	−18	+108
0.8163	0.8513	0.7689	1.5273	1.0101	+ 26	− 8	+ 73
1	1	1	1.5427	0.9698	–	–	–
			Tetralin – carbon tetrachloride				
0	0	0	1.4605	1.5937	–	–	–
0.2045	0.2970	0.2302	1.4872	1.4113	+ 99	+ 23	+ 78
0.3969	0.5196	0.4337	1.5059	1.2726	+ 128	+ 27	+ 98
0.6129	0.7223	0.6482	1.5221	1.1451	+ 112	+ 22	+ 83
0.8270	0.8871	0.8475	1.5343	1.0415	+ 58	+ 9	+ 42
1	1	1	1.5427	0.9698	–	–	–
			Benzene – butyl bromide				
0	0	0	1.4397	1.2740	–	–	–
0.1977	0.2632	0.3018	1.4546	1.1686	+ 28	−13	−36
0.4293	0.5216	0.5689	1.4701	1.0662	+ 41	−16	−45
0.6198	0.7026	0.7409	1.4812	0.9948	+ 35	−17	−40
0.8114	0.8619	0.8830	1.4915	0.9324	+ 20	−11	−24
1	1	1	1.5011	0.8788	–	–	–

The mixtures were prepared in quantities of 20-30 g, and for the 40 and 60% mixtures, weighed portions of pure components (to an accuracy of 1 mg) were taken, while the 20 and 80% mixtures were obtained by dilution of the 40 and 60% by the corresponding components. Re-evaluation of weight units to volume and molar was

carried out by the use of special tables $\log\frac{x}{1-x}$ [16].

Preparation of samples of benzene, mesitylene and 2,2,4-trimethylpentane was the same as used by the author in the preceeding works [17, 18]. Technical tetralin was purified from naphthalene impurity by picric acid treatment, followed by vacuum distillation on a column in vacuo (12 theoretical plates). The main fraction with b.p. 93-93.5° at 20 mm was used. n-Pentane (b.p. 35.4-35.9° at 742 mm) was isolated by treatment with sulfuric acid and distillation on a column of a pentane fraction which was kindly supplied by B.A. Bolotov, to whom the author expresses due acknowledgment. Pure market samples of halogen derivatives were dried and distilled in a column.

The refractive index was measured with a refractometer of the Abbe type (Hilger model, year 1948), the scale of which was adjusted in the working range against the readings of a Billingham-Stanley precision refractometer, and was found to be accurate to $1\text{-}2\cdot10^{-4}$. Thermostat accuracy was $\pm0.05°$.

Density was determined in Regnault and Byron pycnometers, from 5 to 25 ml in volume.

The benzene-2,2,4-trimethylpentane system was investigated earlier by the author [17]; experimental data for the remaining six systems are given in Table 2.

The author takes occasion to express appreciation to Z. L. Sergeeva for assistance in completion of the work.

SUMMARY

1. The problem of substantiation for the additivity rule of refractive indexes has been investigated, and conditions for solution of this problem by experimental procedure have been indicated.

2. The accepted assumptions of refractive index additivity as a function of the molar and weight proportions, which appear in a majority of the works dealing with the refractometric method of physico-chemical analysis, are inaccurate. The isotherms n–N and n–P for non-interacting, non-associated liquid mixtures may have considerable curvature, depending upon the relation between their molar volumes and densities. The explanation of the n–N and n–P isotherm curvature as being due to the interaction or dissociation of the components is for the most part inaccurate. Deductions in old works, which were founded on an interpretation of $\Delta n(N)$ and $\Delta n(P)$ values, are in need of revision.

3. The statement that in ideal system the refractive index as a function of the volumetric proportions of the constituents is additive is more correct (though not completely rigorous). The small curvature for the n–V isotherms in systems approximating ideality is related to the volume changes which occur upon mixing, but the volume change cannot be considered the only cause of deviation from additivity $\Delta n(V)$.

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NEW REDOX INDICATORS

IV. DIPHENYLAMINO-4-SULFO-2-CARBOXYLIC ACID

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In the preceding works [1,2,3] certain diphenylaminocarboxylic acids were synthesized and tested in the capacity of redox indicators. From derivatives of these acids it was first planned to investigate, in the role of redox indicator, diphenylamino-4-sulfo-2′-carboxylic acid in the form of its sodium and potassium salts, which are described in the literature. The sodium salt was obtained from o-chlorbenzoic and sulfanilic acids [4], and the potassium salt from p-brombenzenesulfonic acid and anthranilic acid [5]. However, upon repeating the first synthesis, it turned out that the substance described is apparently the sodium salt of primary sulfanilic acid. Therefore, a special synthesis of diphenylamino-4-sulfo-2′-carboxylic acid had to be carried out, during which great difficulties were encountered in connection with separation of the free acid. Isolation of the acid was greatly facilitated by its property of producing coloration with dichromate in acid medium, which enabled one to judge the quantity of acid present during various stages of the separation.

Diphenylamino-4-sulfo-2-carboxylic acid was synthesized by heating the sodium salts of o-chlorbenzoic acid and sulfanilic acids with potash in nitrobenzene or isoamyl alcohol in the presence of copper powder, during which there was simultaneously observed considerable resinification of the reaction mixture. Better results were obtained when the reaction was carried out in aqueous medium in a sealed tube.

Diphenylamino-4-sulfo-2′-carboxylic acid failed to separate as neutral sodium, potassium and barium salts, since the corresponding salts of the initial sulfanilic acid possess the same solubility; diphenylamino-4-sulfo-2′-carboxylic acid precipitated along with sulfanilic acid during precipitation from reaction mixture by hydrochloric or sulfuric acids. Upon further study it was found that the solubility of diphenylaminosulfocarboxylic acid decreased to a minimum at first, with an increase in concentration of hydrochloric acid, but with further increase in hydrochloric acid concentration the solubility of diphenylaminosulfocarboxylic acid increased sharply, and with still higher concentrations again decreased, and sharply.

The first solubility minimum is explained on the basis of "salting out" with hydrogen ion. The subsequent increase in solubility is explained by salt formation, and the final decrease in solubility — by "salting out" with chloride ion. Diphenyl-4-sulfo-2-carboxylic acid was successfully separated from solutions containing the initial sulfanilic acid in the form of the acid barium salt, which in contrast to the sulfanilic acid barium salt was found to be poorly soluble in water.

The free acid was isolated by decomposition of the acid barium salt with sulfuric acid. For characterization of the diphenylaminosulfocarboxylic acid, its sodium and barium salts were obtained, and also the monomethyl ester. In sulfate medium diphenylamino-4-sulfo-2′-carboxylic acid and its methyl ester form an intense blue-violet coloration in the presence of dichromate and cerium sulfate. The coloration is reversibly decolorized by addition of a reducing agent, and both substances, therefore, can be used as redox indicators.

In conclusion, the author wishes to express sincere appreciation to Prof. A.V. Kirsanov for advice in completion of this work.

EXPERIMENTAL

Diphenylamino-4-sulfo-2′-carboxylic acid. 0.05 mole (11.5 g) of sodium sulfanilate, 0.05 mole (9.5 g) of o-chlorbenzoic acid sodium salt, 0.1 g of copper powder and 0.6 g of copper sulfate were heated in five sealed glass tubes with 20 ml of water for 15 hours at 115-120°. The reaction mixture was filtered and the filtrate acidified with hydrochloric acid to an acid reaction with Congo red. The resulting precipitate was filtered off, dried and, to remove o-chlorbenzoic acid it was treated several times with small quantities of ether. The precipitate was treated 3 times with 10 ml portions of water, filtrates combined, and saturated barium chloride solution added to the combined filtrates. The resulting acid barium salt was filtered by suction in the form of a fine crystalline precipitate, washed with water, and dried. Yield 5.2 g, or 28.8% of theoretical.

0.2317 g substance: 0.0065 g H_2O. Found %: H_2O 2.80. $Ba(C_{13}H_{10}O_5NS)_2 \cdot H_2O$. Calculated %: H_2O 2.4
0.2008 g substance: 0.0654 g $BaSO_4$. Found %: Ba 18.58. $Ba(C_{13}H_{10}O_5NS)_2$. Calculated %: Ba 18.51.

To obtain larger quantities, the reaction was carried out in a copper autoclave using 0.5 mole of original acids.

Synthesis of free diphenylamino-4-sulfo-2-carboxylic acid. 5.2 g of the acid barium salt was heated with 10 ml of water and 0.5 ml of concentrated sulfuric acid on a water bath. The hot solution was filtered, brought to 20 ml volume, and 7 ml of hydrochloric acid, spec. grav. 1.19, used to acidify for precipitation of the diphenylaminosulfocarboxylic acid. Solubility of the diphenylaminosulfocarboxylic acid is minimal at a solution acidity corresponding to a hydrochloric acid content of about 20%. The resulting precipitate was filtered off with suction, washed with 20% hydrochloric acid solution and dried over caustic potash, and then sulfuric acid. Repeated purification of the product was carried out by dissolution in water and by precipitation with concentrated hydrochloric acid.

The product failed to crystallize from water because of the very high solubility. The substance dissolves in alcohol upon heating, and crystallizes well, but cannot be filtered off with suction since it is of a consistency resembling gel.

The diphenylaminosulfocarboxylic acid resulting from precipitation with hydrochloric acid is flaky, with a greenish hue, greasy to the touch; difficultly soluble in ether and benzene, decomposes on heating, without melting.

0.3066 g substance: 0.0336 g H_2O. 0.3669 g substance: 22.3 ml 0.1 N KOH. Found %: H_2O 10.83; M 328.8. $C_{13}H_{11}O_5NS \cdot 2H_2O$. Calculated %: H_2O 10.94; M 329.0. 10.18 mg substance: 0.411 ml N_2 (14°, 732 mm). Found %: N 4.62. $C_{13}H_{11}O_5NS$. Calculated %: N 4.77.

Diphenylamino-4-sulfo-2'-carboxylic acid salts. Neutral barium salt. 0.2 g of barium carbonate was added to 2.93 g of the acid dissolved in 15 ml of water. The mixture was heated on a water bath and filtered. After evaporating in vacuo, the residue yielded colorless needles, readily soluble in water, poorly soluble in alcohol.

0.2046 g substance: 0.0164 g H_2O. Found %: H_2O 7.93. $C_{13}H_9O_5NSBa \cdot 2H_2O$. Calculated %: H_2O 7.74. 0.1655 g substance: 0.0898 g $BaSO_4$. Found %: Ba 31.87. $C_{13}H_9O_5NSBa$. Calculated %: Ba 32.08.

Acid sodium salt. 0.53 g of soda ash was added to a solution of 2.93 g of the acid in 5 ml of water. The resulting fine, colorless crystals were filtered off with suction and washed with water. The salt was poorly soluble in water, insoluble in alcohol.

0.4994 g substance: 0.0065 g H_2O. Found %: H_2O 5.60. $C_{13}H_{10}O_5NSNa \cdot H_2O$. Calculated %: H_2O 5.40. 0.2011 g substance: 0.0446 g Na_2SO_4. Found %: Na 7.08. $C_{13}H_{10}O_5NSNa$. Calculated %: Na 7.30.

Neutral sodium salt. 1.06 g of soda in 5 ml of water, as a solution, was added to 2.93 g of the acid dissolved in 10 ml of water. A precipitate of acid salt resulted, which then dissolved completely. The solution was evaporated to dryness in vacuo. After repeated recrystallization from aqueous alcohol, colorless crystals resulted, readily soluble in water, difficultly-soluble in alcohol.

0.2070 g substance: 0.0103 g H_2O. Found %: H_2O 4.97. $C_{13}H_9O_5NSNa_2 \cdot H_2O$. Calculated %: H_2O 5.07. 0.1914 g substance: 0.0788 g Na_2SO_4. Found %: Na 13.66. $C_{13}H_9O_5NSNa_2$. Calculated %: Na 13.32

Monomethyl ester of diphenylamino-4-sulfo-2'-carboxylic acid. 5.04 g of dimethyl sulfate was added to a solution of 1.46 g of diphenylaminosulfocarboxylic acid in 15 ml of 10% caustic soda, the mixture shaken for 15 minutes, and then acidified with hydrochloric acid. The resulting precipitate was aspirated and washed with water. After recrystallization from aqueous alcohol – colorless crystals resulted, readily soluble in alcohol. The barium salt of the methyl ester was difficultly soluble in water. The melting point was not determined, since the above substance decomposed without melting.

10.43 mg substance: 0.420 ml N_2 (15°, 732 mm). Found %: N 4.51. $C_{14}H_{13}O_5NS$. Calculated %: N 4.56.

To test diphenylamino-4-sulfo-2'-carboxylic acid as a redox indicator, 0.001N solutions of potassium dichromate, cerium sulfate and 0.001M solution of the indicator were used. The total volume of the solutions during testing was 100 ml.

Upon oxidation, the color of diphenylaminosulfocarboxylic acid changed from colorless through yellow-green to a pure blue-violet.

Determination of the acidity range (the lowest normality of sulfuric acid in the solution) at which titration is possible. The dichromate and indicator solutions were added in 4 ml portions to 100 ml of sulfuric acid solutions of varying normality. A suitable color for titration appeared immediately in 10N sulfuric acid solution. At lower solution acidity the color appeared after a certain time. Where ceric sulfate was used, an intense color appeared in 2N sulfuric acid solution; however, this color was less stable: fading rapidly and vanishing.

The smallest quantity of oxidizer and indicator solution possible in 10N sulfuric acid solution at which titration remained possible was 2 ml (optimal quantities 4 ml).

An increase in volume of indicator in the solution above a certain limit did not intensify the color, but imparted a yellowish shade to it. If ferrous ions are present in the solution, then a change in color of the indicator, due to dichromate excess, occurs at lower acidity – in 7.5N sulfuric acid solution.

The possibility for practical application of diphenylaminosulfocarboxylic acid in the capacity of a redox indicator was verified by parallel titration of Mohr's salt solutions along with titration in the presence of known indicators – diphenylaminosulfonic acid and phenylanthranilic acid – at which time deviations in results were observed. Use of large quantities of the indicator should be avoided since it leads to large indicator errors. The latter circumstance does not permit determination of the redox potential for diphenylaminosulfocarboxylic acid.

Properties of the monomethyl ester, as a redox indicator are hardly distinguishable from the properties of diphenylaminosulfocarboxylic acid.

SUMMARY

1. Diphenylamino-4-sulfo-2'-carboxylic acid has been synthesized.

2. It has been demonstrated that diphenylamino-4-sulfo-2'-carboxylic acid may be used in the role of redox indicator when working with strong oxidants.

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CATALYTIC THERMOPOLYMERIZATION OF ISOBUTYLENE UPON QUARTZ AT LOW PRESSURES

A. D. Stepukhovich and F. M. Mitenkov

During the course of experiments on the thermal decomposition of isobutylene in the region of low pressures and in a temperature range of 811-828° K, in which a spherical quartz flask served as the reactor, the authors encountered an interesting phenomenon. At isobutylene pressures below 2 mm, rather than an increased pressure in the reactor as the result of isobutylene decomposition, a noticeable decrease in pressure was observed instead within the first two minutes, which in some experiments dropped to 20% of the initial pressure. In Table 1 are given data for the influence of initial isobutylene pressure upon the magnitude of relative decrease in pressure within the first two minutes at pressures below 2 mm. As can be seen, the smaller the initial pressure of isobutylene, the greater is the decrease in pressure. The most probable explanation for this fact, in the authors' opinion, is the assumption of isobutylene polymerization which, at these pressures, predominates over the decomposition reaction.

TABLE 1

Pressure Change with Time During the Isobutylene Decomposition Reaction

Test	P_0 (mm)	Per cent pressure change* for same reaction time									
		2 min.	4 min	6 min.	8 min.	10 min.	12 min.	14 min.	16 min.	18 min.	20 min.
						T = 811° K					
15	0.44	- 20.85	- 20.85	- 20.85	- 18.93	- 17.66	—	—	—	—	—
13	0.63	- 18.46	- 18.46	- 18.46	- 17.11	- 16.01	- 15.46	—	- 12.42	—	- 11.58
12	0.85	- 17.14	- 14.79	- 12.41	- 10.04	- 9.99	- 7.55	- 6.55	- 4.31	- 2.55	- 0.51
9	1.29	- 4.13	- 2.09	+ 2.09	+ 5.1	+ 8.49	—	—	—	—	—
17	1.68	- 2.55**	—	—	—	—	—	—	—	—	—
						T = 816° K					
26	0.65	- 16.87	- 14.27	- 14.27	- 8.91	- 7.94	- 5.94	- 2.92	- 2.34	0	+ 2.96
18	1.21	- 8.41	- 6.97	- 4.16	- 2.14	0	+ 2.6	+ 4.35	—	—	—
21	1.86	- 0.86	+ 1.58	+ 3.51	+ 7.09	+ 9.98	+12.55	+14.41	+18.15	+18.54	+20.05
						T = 828° K					
31	0.94	- 5.99	- 3.89	- 0.49	+ 1.23	+ 3.88	+ 6.19	+ 9.98	+12.06	—	—
32	1.08	- 8.06	- 5.65	- 1.37	+ 1.13	+ 3.88	+ 5.78	+ 8.15	+10.54	—	—

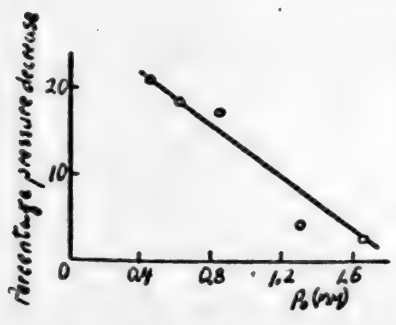

Fig. 1. Relation of Pressure Decrease to Initial Isobutylene Pressure at 811°K.

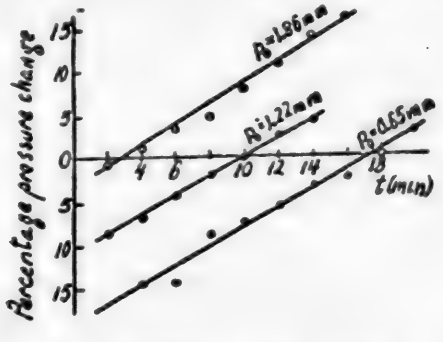

Fig. 2. Relation of Pressure Change to Reaction time for Isobutylene Decomposition (T = 811°K).

The polymerization of isobutylene at pressures below 2 mm of mercury evidently occurs on the walls of the quartz reactor, and appears to be a heterogeneous-catalytic process. The validity of this assumption is indicated by Fig. 1 which shows that the percentage pressure decrease falls to zero, at the same time that the pressure increases to approximately 2 mm,

* "-" sign indicates pressure decrease, and "+" sign its increase. ** Further for the 5th, 7th, 9th ... 17th minutes respectively: +0.73, +2.94, +4.81, + 6.68, +8.59, +12.1, +12.43.

and at higher pressures only decomposition takes place, which is accompanied by a pressure increase. As is known, normal polymerization is a homogeneous and bimolecular reaction, and with pressure increase should increasingly prevail over decomposition, due to the fact that pressure would continue to decrease with further increase in primary pressure.

Meanwhile, in the authors' experiments, polymerization is in no way manifested at pressures above 2 mm. Moreover, if it is assumed that under the authors' experimental conditions a normal polymeriz ation takes place, then it appears impossible to explain the initial pressure change in that period of time when the pressure is below 2 mm. The data given in Table 1 indicate that the pressure decrease occurs only within the first two minutes of the reaction, but after that the pressure increases almost linearly with time, as is shown in Figs. 2 and 3. Thus the process which conditions the pressure decrease occurs and is completed within the first two minutes of reaction. After that only isobutylene decomposition proceeds, the rate of which conforms to a first order reaction equation.

The facts which have been discussed lead to the conclusion that at pressures below 2 mm, in the temperature range 811-828° K, catalytic polymerization of isobutylene occurs on the walls of the quartz reactor. We shall now attempt to present a hypothetical picture of this phenomenon. It might be assumed that because of adsorption, the surfaces of the walls are covered with a layer of isobutylene molecules, in all probability of monomolecular layer thickness, upon introducing the gas into the evacuated reactor. Upon impacts of isobutylene molecules with those sections of the walls which are covered with isobutylene molecules, promotion of molecular polymerization may occur due to heterogeneous catalysis.

During the first moments of time this process proceeds so rapidly that the pressure decrease caused by it considerably exceeds the pressure increase which is simultaneously conditioned by the occurrence of isobutylene molecular decomposition. The catalytic polymerization phenomenon, under the experimental conditions defined by the authors, may perhaps take place at any initial pressure. However, at pressures above 2 mm, this process is completed so rapidly that the pressure decrease does not become evident in the experiments. At lower initial pressures the catalytic polymerization rate is smaller, and for its completion requires correspondingly longer time. As a first approximation, this time is inversely proportional to the initial pressure. As the active parts of the surface (or the whole surface) of the reactor become covered with a layer of forming isobutylene polymers, catalysis of polymerization ceases, decomposition begins to predominate, and consequently the increase in pressure within the reactor will begin.

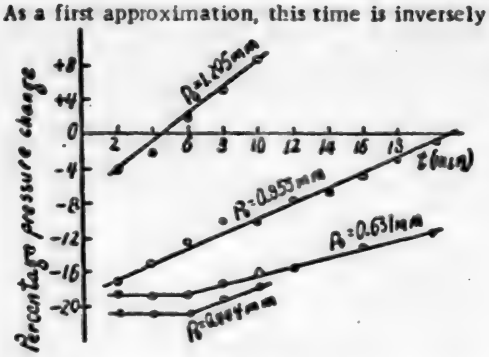

Figure 3. Relation of Pressure Change to Time During Isobutylene Decomposition (T = 813°K).

Actually, after lapse of the first two to four minutes, within which time the pressure decrease takes place, a gradual increase in pressure was observed which was proportional to the reaction time. In addition, having made certain assumptions, it can be demonstrated that the proposed explanation is in quantitative agreement with the experimental data. Let it be assumed that the rate of catalytic polymeri ation on the wall is defined by the equation

$$W = K^1 X, \qquad (1)$$

in which X = volume concentration of isobutylene and K^1 = the polymerization rate constant, which does not depend upon the concentration of isobutylene, but changes in the course of time up to zero (or to a very small value). It will be considered that K^1 is constant up to a certain moment of time (depending upon the initial pressure), starting from which the constant K^1 assumes a value of zero. This simplification will permit a comparison with experiment. The K^1 value can be calculated from the number of isobutylene molecular impacts with the reactor walls, if the simplified assumption is made that the entire wall surfaces participate in catalysis. For calculation of the K^1 value, the following expression was used:

$$K^1 = \frac{1}{4} a S \left(\frac{2\pi kT}{m}\right)^{\frac{1}{2}} e^{-\frac{E-\epsilon}{kT}} \qquad (2)$$

in which S = square surface area of the reactor walls (cm^2); E = activation energy for the homogeneous isobutylene polymerization reaction; ϵ = the gain in energy, conditioned by the catalyst action; a = a steric factor. According to the calculations for isobutylene polymerization [1]: E = 42 kcal./mole, and $a = 7 \cdot 10^{-3}$.

Using the radius value for the spherical reactor (r = 4 cm), and assuming that E = 10 kcal./mole, a K^1 = value of 0.00043 was obtained at 811°K.

If K_1 = the monomolecular isobutylene decomposition constant, then the concentration change resulting from the two competing processes per unit of time is equal to $\Delta X = (K^I - K_1)X_1$, and for a time interval of Δt respectively $\Delta X \cdot \Delta t = (K^I - K_1)X\Delta t$. Here an assumption will be made concerning the constancy of K^I up to a certain moment in time. The percentage pressure decrease for Δt time can be calculated, which is equal to

$$\frac{\Delta p}{p} \cdot 100 = \frac{\Delta X \cdot KT}{p} \Delta t \cdot 100 = \frac{(K^I - K_1)\, X\Delta t KT}{p} \cdot 100. \qquad (3)$$

Apparently if the pressure change becomes negative by the use of (3), then this indicates that at this moment in time an increase in pressure will result, instead of a pressure decrease, and that decomposition will predominate over polymerization.

TABLE 2

T°K	p_0(mm)	reaction time (in min.)	pressure decrease (%)	
			calculated	experimental
811	1.68	2	3.18	2.55
811	1.29	2	4.36	4.13
811	0.63	6	14.30	18.46
811	0.44	6	14.66	20.85
828	1.08	2	6.93	8.10
828	0.94	2	6.80	6.00

A comparison is given in Table 2 of the calculated and of the experimental pressure drops at an initial pressure below 2 mm of mercury. At the moment in time, t, starting from which, according to the assumption made, K^I can be considered equal to zero, the authors selected this moment of time, experimentally, as that moment at which the pressure decrease is replaced by an increase. Using K_1, calculated values for constants at corresponding isobutylene pressures were taken as (811° K and $p_0 = 1.68$): $K_{1calc.} = 3.76 \cdot 10^{-4}$; $p_0 = 1.29$; $K_{1calc.} = 6.87 \cdot 10^{-4}$ and so forth. (828°K and $p_0 = 1.08$): $K_1 = 0.87 \cdot 10^{-4}$; $p_0 = 0.94$, $K_1 = 0.77 \cdot 10^{-4}$.

SUMMARY

1. In the pressure region below 2 mm, at a temperature between 811-828°K, a catalytic thermopolymerization of isobutylene occurs on the quartz walls, which predominates over decomposition in this range.

2. A hypothetical mechanism for catalytic thermopolymerization of isobutylene for pressures below 2 mm has been given, which agrees satisfactorily with the facts.

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SULFOCHLORINATION

I. THERMAL DECOMPOSITION OF ALKANESULFONIC ACID CHLORANHYDRIDES AS A METHOD FOR DETERMINATION OF POSITION OF THE SULFO GROUP

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Within the past few years the method of introducing the sulfonic acid group into paraffins and cycloparaffins by the action of sulfur dioxide and chlorine with exposure to short wave-length light has gained wide application both in the laboratory and in industrial practice. During this reaction a mixture of the chloranhydrides of the mono- and disulfonic acids results, which is why it is frequently called a sulfochlorination reaction [1].

Determination of the place of entry of the sulfo group offers considerable difficulty since the aliphatic sulfonic acds have received but little study up to the present time; moreover, the sulfochlorides themselves are quite unstable, and distill without decomposition only in vacuo (n-octanesulfonylchloride, and larger molecules distill with decomposition even in vacuo). It is known that [1] upon distillation without vacuum a sulfonyl chloride decomposes readily to form sulfur dioxide and hydrogen chloride and also to form chlorides and olefins. However, up to the present time no systematic study of this reaction has been carried out.

The authors' experiments cited below, for decomposition of several mono- and dichloranhydrides, have shown that in all cases chlorine enters only that position which is occupied by the sulfo group in the initial compound.

The following sulfochlorides were investigated:

1) $CH_3CH_2CH_2CH_2SO_2Cl$ – chloranhydride of butanesulfonic-1-acid;
2) $(CH_3)_2CHSO_2Cl$ – chlorznhydride of propanesulfonic-2-acid;
3) $(CH_3)_2CHCH_2SO_2Cl$ – chloranhydride of 2-methylpropanesulfonic acid;
4) $C_6H_5CH_2CH_2SO_2Cl$ – chloranhydride of ethylbenzosulfonic-1[2]-acid;
5) $CH_2(SO_2Cl)CH_2CH_2CH_2SO_2Cl$ – dichloranhydride of butanedisulfonic-1,4-acid;
6) $CH_2(SO_2Cl)CH_2CH(SO_2Cl)CH_3$ – dichloranhydride of butanedisulfonic-1,3-acid.

The monochloranhydrides were synthesized from the corresponding chlorides by conversion to the rhodanides, with subsequent treatment of the latter by chlorine. The chloranhydrides were characterized by the melting points of their amides. The dichloranhydrides were synthesized by sulfochlorination of the chloranhydrides of butane-sulfonic-1-acid with exposure to a mercury lamp. From the resulting mixture two isomers were isolated, and their melting points determined. It should be mentioned that according to the literature data [2], the fatty chloranhydrides give very low yields of amides (25-30%) upon treatment with gaseous ammonia. For this purpose the authors recommend amidation by the use of liquid ammonia [3]. By this method, in the authors' experiments, high amide yields (up to 90%) invariably resulted.

Decomposition of sulfochlorides begins above 100°; however, the rate is negligible up to 150-160°. The authors carried the reaction out in an oil bath of 200-220° temperature. Reaction was complete within 1.5-2 hours. The reaction flask was equipped with a reflux condenser filled with hot water of such temperature that the highly volatile chloride formed could be distilled. In this manner the chloride yields were considerably increased (up to 75-85%). For the dichloranhydrides, the reflux condenser was replaced by a fractionating column. The chlorides isolated from the reaction boiled within narrow ranges. They were identified by their boiling points and specific gravities.

In addition, each of the resulting chlorides was then converted into the rhodanide, the chloranhydride, and the corresponding sulfonamide. The latter, by mixed melting point tests, were identified as the chloranhydrides obtained by decomposition. It was thus proved with certainty that an exchange of the SO_2Cl group for the chlorine atom occurs at the same position on the carbon chain without isomerization.

The transformation reaction studied by the authors may be of considerable aid in determining the structure of fatty sulfonic acids. The latter have been but little studied up to the present time; however, the chlorides are known for a great number of various representatives, with well-defined constants, and can be further characterized by conversion into compounds of other classes.

EXPERIMENTAL

Synthesis of Sulfonylchlorides

The Chloranhydride of Propanesulfonic-2-acid. 230 g (2.34 moles) of potassium rhodanide was added to 150 g (1.9 moles) of 2-chlorpropane (d_4^{20} 0.8588; b.p. 36-37°) which was dissolved in 500 ml of ethyl alcohol. The mixture boiled with reflux for 40 hours on a water bath. The reaction mixture was diluted with water. The rhodanide was extracted with ether. The ether extract was washed with water and dried with calcium chloride. After removal of ether, the 2-rhodanepropane was distilled; b.p. 148-150° (745 mm). 160 g resulted (yield 83.3%; d_4^{20} 0.9784.

155 g of 2-rhodanepropane and 1.5 liters of water were introduced into a three-necked, three-liter flask, equipped with stirrer, bubbler for chlorine, and a thermometer. With a continuously operating stirrer, chlorine was let in at such a rate that the reaction mixture temperature did not exceed 20°. Reaction continued until the reaction mass turned yellow from chlorine excess. After completion of reaction, chlorine was removed by a stream of nitrogen. The resulting chloranhydride (a heavy oil of sharp odor) was extracted with ether, and dried with calcium chloride. The chloranhydride was redistilled in vacuo (yield 83.2%). B.p. 71-73° (13 mm). (According to Düge [4], b.p. 79° at 18 mm; d_4^{20} 1.1645.

Found %: Cl 24.81, 24.89. $C_3H_7O_2ClS$. Calculated %: Cl 24.91.

The Amide of Propanesulfonic-2-acid. This was obtained in the following manner: 10.2 g (0.072 mole) of the chloranhydride was dissolved in 50 ml of ether, cooled to −40° with alcohol-dry ice mixture, and then added gradually to liquid ammonia (11 g) which was cooled to the same temperature, and placed in a Dewar flask. The mixture was left for 8-10 hours at normal temperature, and was then heated on a water bath to remove ammonia. The solution was separated from ammonium chloride by filtration and diluted with petroleum ether. The resulting amide was recrystallized from ether and petroleum ether mixture. 8.02 g resulted (yield 91.2%). White flakes, m.p. 66° (according to Düge [4], m.p. 60°).

Found %: S 25.97, 25.93. $C_3H_9O_2NS$. Calculated %: S 26.01.

The Chloranhydride of Butanesulfonic-1-acid. 377 g (3.88 moles) of potassium rhodanide was added to a solution of 300 g (3.24 moles) of 1-chlorbutane in 1200 ml of ethyl alcohol. The mixture was boiled on reflux for 60 hours. Processing of the mixture was carried out as above. 281.9 g (75.8) of 1-rhodanebutane resulted. B.p. 182-183°.

Conversion of the rhodanide into chloranhydride was carried out as described for 2-rhodanepropane above. 330.6 g (90% of theoretical) of the chloranhydride of butanesulfonic-1-acid resulted from 270 g of rhodanebutane. B.p. 75-76° (7 mm); d_4^{20} 1.2078. (According to Düge [4], b.p. 96-97° at 18 mm).

Found %: Cl 22.63, 22.67. $C_4H_9O_2ClS$. Calculated %: Cl 22.68.

The Amide of Butanesulfonic-1-acid. This was prepared, as described above for the amide of propanesulfonic-2-acid, from 8.5 g of the chloranhydride of butanesulfonic-1-acid. There was obtained 6.13 g (82.4% of theoretical) of the amide. After recrystallization from a mixture of ethyl and petroleum ethers – white flakes with m.p. 44-44.5° (according to Düge [4], m.p. = 45°).

Found %: 23.32, 23.29. $C_4H_{11}O_2NS$. Calculated %: S 23.35.

The Chloranhydride of 2-Methylpropanesulfonic-1-acid. 133.4 g of potassium rhodanide was added to a solution of 200 g (1.46 moles) of isobutyl bromide in 600 ml of ethyl alcohol. The mixture was boiled with a reflux for 16 hours on a water bath. The reaction mass was processed as before. 123.2 g of 1-rhodane-2-methylpropane resulted (73.2% yield. B.p. 57-58.5°, 8 mm).

The chloranhydride of 2-methylpropanesulfonic-1-acid was obtained from the rhodanide by the action of chlorine, as indicated above. From 115.0 g of rhodanide, 132.0 g (84.0% of theoretical) sulfonyl chloride resulted. B.p. 77-78° (11 mm); d_4^{20} 1.2014 (according to Düge [4], 79.5-80° at 13 mm).

Found %: Cl 22.52, 22.57. $C_4H_9O_2ClS$. Calculated %: Cl 22.68.

Since the amide of 2-methylpropanesulfonic-1-acid is a liquid at normal conditions (according to Düge [4], b.p. = 14-16°), for identification, therefore, the authors used the crystalline cyclohexylamide. 3.0 g of sulfonyl chloride was dissolved in 20 ml of ether, and 8.2 g of cyclohexylamide was added to the solution. The mixture was boiled for 6 hours on a water bath with a reflux condenser. The precipitated hydrochloride of cyclohexylamine was filtered off. After washing with dilute hydrochloric acid, the residue after evaporation of the ether was recrystal-

lized from methyl alcohol. 2.81 g of white needle crystals resulted, with m.p. 56-57°.

Found%: S 14.31, 14.39. $C_{10}H_{12}O_2NS$. Calculated %: S 14.66.

The Chloranhydride of Ethylbenzenesulfonic-1[2]-acid. 26.10 g (0.27 mole) of potassium rhodanide was added to a solution of 25 g (0.18 mole) of 1[2]-chlorethyl benzene in 150 ml of ethyl alcohol. The mixture was boiled on a water bath under reflux for 40 hours. Processing of the reaction mixture was carried out as before.

19.26 g (66.4% of theoretical) of the 1[2]-rhodaneethylbenzene resulted. B.p. 116-118° (3 mm); d_4^{20} 1.2158.

Found %: S 19.58, 19.54. C_9H_9NS. Calculated %: S 19.63.

Conversion of the rhodanide into the sulfonylchloride was carried out with the chlorine treatment as described above. The viscous liquid resulting from the reaction was extracted with ether. The extraction was washed with water and dried with calcium chloride. After evaporation of the ether, the residue partially crystallized on standing. The pressed-out crystals were recrystallized from benzene and petroleum ether mixture. From 16.34 g of rhodaneethylbenzene, 10.45 g (51.10%) of long, colorless flakes, with m.p. 81-82°, resulted.

Found %: Cl 17.29, 17.32; S 15.52, 15.56. $C_8H_9O_2ClS$. Calculated %: Cl 17.35; S 15.64.

The amide was obtained as above. From 1.2 g of sulfonyl chloride 0.72 g (66.3%) of the amide resulted. After recrystallization from hot water – white, fine needle crystals with m.p. 129-129.5°.

Found %: S 17.24, 17.18. $C_8H_{11}O_2NS$. Calculated %: S 17.29.

The Dichloranhydrides of Butanedisulfonic-1,4-and Butanedisulfonic-1,3-acids. 126.0 g of the chloranhydride of butanesulfonic-1-acid was placed in a three-necked flask equipped with stirrer, bubbler and thermometer, and was treated for 10 hours with a mixture of gaseous chlorine and sulfur dioxide, with exposure to a mercury lamp SVD Sh-250. Chlorine was introduced at the rate of 0.8 ml/sec., the sulfur dioxide – 1.3 ml/sec. At first the reaction mass became green-colored, but decolorized after 20 minutes and remained so to the end of the reaction. The temperature rose from 20 to 40° and was maintained unchanged up to the end of the gas introduction. After 10 hours introduction of gas was complete, and the excess gases were removed by a stream of nitrogen. 173.0 g of colorless oil resulted. The reaction product was fractionally distilled in vacuo. 119.4 g distilled at 60-80° (8mm). The residue in the flask amounted to 50.3 g. The residue, which solidified to a brown crystalline mass, was dissolved in 100 ml of benzene, and was boiled with activated charcoal under reflux to decolorize. During precipitation of the filtrate with carbon tetrachloride, crystals resulted which were then recrystallized from benzene and petroleum ether mixture. 41.2 g of white needles with m.p. 82.5-83° resulted. From its melting point, the resulting substance corresponded to the dichloranhydride of butanedisulfonic-1,4-acid (according to Asinger [7], m.p. = 83.5°.)

Found %: Cl 27.76, 27.71. $C_4H_8O_4Cl_2S_2$. Calculated %: Cl 27.84.

200 ml of petroleum ether was added to the filtrate from the preceding operation. The precipitated crystals were filtered off and recrystallized from benzene and petroleum ether. 6.3 g of white needles with m.p. 40-41° resulted. From its melting point, the substance corresponded to the dichloranhydride of butanedisulfonic-1,3-acid (according to Asinger [7], m.p. = 41°.)

Found %: Cl 27.68, 27.71. $C_4H_8O_4Cl_2S$. Cl 27.84.

Thermal Decomposition of the Chloranhydrides of Sulfonic Acids.

The authors used the following apparatus for decomposition of the monosulfonyl chlorides. The reaction flask was connected by a ground connection to a vertial condenser filled with hot water in such a manner that the chloride vapors forming during the reaction passed on through the condenser. The gases and vapors formed entered into a descending condenser. The condensate was collected in a receiver and trap placed in a Dewar flask filled with water and ice. In experiments with the dichloranhydrides and chloranhydrides of ethylbenzenesulfonic acid, the vertical condenser was replaced by a fractionating column 20 cm in length wrapped with two layers of asbestos.

The Chloranhydride of Propanesulfonic-2-acid. 20 ml (25.28 g) of the chloranhydride of propanesulfonic-2-acid was charged into the reaction flask. The decomposition was carried out at an oil bath temperature of 200-220°. Reaction was complete after 1.5 hours. The combined condensate from receiver and trap was subsequently washed with 3% soda solution and water. After drying with calcium chloride, 10.5 g of the chloride resulted (yield 73.4% of theoretical). B.p. 36-37°; d_4^{20} 0.8565 (according to Leca [5], the b.p. = 36.25° at 760 mm).

Found %: Cl 45.16, 45.15. C_3H_7Cl. Calculated %: Cl 45.22.

For confirmation of the structure of the obtained chloride, it was subsequently converted into the rhodanide, the sulfonyl chloride, and the sulfonamide. The latter was found to be identical with the amide of propanesulfonic-2-acid: m.p. 65-66°, and with no melting point depression for the mixture.

The Chloranhydride of Butanesulfonic-1-acid. Decomposition of the chloranhydride and treatment of the obtained chloride were carried out similarly to that described above for the chloranhydride of propanesulfonic-2-acid. 12.43 g of the chloride (yield 87.9% of theoretical) was obtained from 20 ml (24.16 g) of the chloranhydride of butanesulfonic-1-acid. B.p. was 77-78°; d_4^{20} 0.8892 (according to Leca [5], b.p. = 78.05° at 760 mm).

Found %: Cl 38.28, 38.29. C_4H_9Cl. Calculated %: Cl 38.37.

For confirmation of the structure, the chloride obtained was converted to the amide of butanesulfonic acid with m.p. 44-45°.

A sample of the obtained amide when mixed with the amide from initial chloranhydride of butanesulfonic acid did not show depression in the melting point.

Chloranhydrideof 2-methylpropanesulfonic-1-acid Decomposition of the sulfonyl chloride and treatment of the obtained chloride was carried out in a manner similar to the preceding cases. 5.95 g of chloride resulted (yield 79.63% of theoretical) from 12.7 g of the chloranhydride of 2-methylpropanesulfonic-1-acid. B.p. was 68-69°, d_4^{20} 0.8800 (according to Linnemann, b.p. = 68.5°).

Found %: Cl 38.34, 38.25. C_4H_9Cl. Calculated %: Cl 38.37.

For confirmation of the structure of the obtained chloride, it was converted into the sulfonyl chloride and then into the cyclohexylamide. After recrystallization from methyl alcohol, it was in the form of fine needles, m.p. 56-57°. Melting test for the mixture also confirmed the identity with cyclohexylamide of 2-methylpropanesulfonic acid.

Dichloranhydride of butanedisulfonic-1,4-acid. Decomposition was carried out at an oil bath temperature of 200-221°. The chloride formed was subsequently washed with sulfuric acid (d. 1.84) and water. From 5.02 g of disulfonylchloride, 1.98 g of the chloride resulted (yield 79.1% of theoretical). M.p. 155-156° (according to Sivolobov) d_4^{20} 1.1633.

Found %: Cl 55.80, 55.89. $C_4H_8Cl_2$. Calculated %: Cl 55.90.

For the determination of structure, 1 g of the obtained dichloride was dissolved in 20 ml of alcohol, and 3 g of potassium rhodanide was added to the solution. The mixture was boiled on reflux for 40 hours on a water bath. After dilution of the mixture with water, the dirhodanide was extracted with ether, and after removal of the ether and alcohol traces on a water bath, the residue was suspended in 20 ml of water and treated with chlorine as described above. The chloranhydride precipitated during the reaction in the form of white flakes. From the melting point (81-82°) and by absence of depression, the identity with the chloranhydride of butanesulfonic-1,4-acid was established.

The Dichloranhydride of Butanedisulfonic-1,3-acid. Decomposition of the dichloranhydride and treatment of the dichloranhydride was carried out similarly to that described above for the 1,4-isomer. 1.15 g of the dichloride resulted (yield 72.5%) from 3.2 g of the dichloranhydride of butanedisulfonic-1,3-acid. B.p. 130-132° (according to Sivolobov), d_4^{20} 1.0849.

Found %: Cl 55.74, 55.62. $C_4H_8Cl_2$. Calculated %: Cl 55.90.

For determination of structure, 0.5 g of the obtained dichloride was converted into the disulfonylchloride in the same manner as with the preceding case. An oil resulted, which crystallized upon standing. Upon recrystallization from benzene and petroleum ether mixture, white needles resulted with a m.p. of 42-43°. The sample of the obtained dichloranhydride, mixed with initial dichloranhydride of butanesulfonic-1,3-acid did not show depression.

The Chloranhydride of Ethylbenzenesulfonic-1[2]-acid. Decomposition of the chloranhydride was carried out in a manner similar to that described above for the dichloranhydrides of butanesulfonic acids. The chloride resulting upon decomposition was subsequently washed with sulfuric acid (d. 1.84) and then with water and dried with calcium chloride. 2.92 g of chloride resulted (59.4% of theoretical) from 7.15 g of the chloranhydride.

Found %: Cl 24.88, 24.96. C_8H_9Cl. Calculated %: Cl 25.56.

For structure determination the obtained chloride was subsequently converted into the rhodanide and sulfonyl chloride, in a manner as above. 0.48 g of sulfonyl chloride resulted from 2.1 g of the chloride. The former, after recrystallization from petroleum ether, had a m.p. of 81-82°. A test of the obtained chloranhydride when mixed with the initial chloranhydride did not show depression.

SUMMARY

1. It has been demonstrated that chlorides result from the thermal decomposition of paraffinic sulfonyl-chlorides (with yield 75-84%), wherein halogen takes the place of the sulfonyl group. The following were taken as objects for investigation: the chloranhydrides of propanesulfonic-2-acid, butanesulfonic-1-acid, 2-methylpropane-sulfonic-1-acid, ethylbenzenesulfonic-1^2-acid and dichloranhydrides of butanesulfonic-1,4- and butanesulfonic-1,3-acids.

2. It has been recommended that the fatty sulfonyl chlorides be converted into the corresponding amides by treatment of ether solutions of the chloranhydrides with liquid ammonia. Amides are obtained with yields 90% of theoretical.

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SULFOCHLORINATION

II. ORIENTING EFFECT OF THE SO_2Cl AND Cl GROUPS DURING PHOTOCHEMICAL SULFOCHLORINATION

A. P. Terentyev and A. I. Gershenovich

In a preceding article by the authors [1], a brief review of contemporary methods for derivation of alkanesulfonyl chlorides, along with proposed methods for the identification and determination of sulfonyl group positions, was given. The latter consists of converting the sulfonyl chlorides into chlorides by heat; at such time, chlorine replaces the sulfonyl group. In the present article the authors have undertaken the task of clarifying certain problems related to the photochemical sulfochlorination process. Up to the present time, the theory on this process has received but little study. As is known, paraffinic hydrocarbons, when reacted with a mixture of sulfur dioxide and chlorine, with exposure to light of short wave length, convert into the chloranhydrides of the sulfonic acids with good yields; at the same time, direct chlorination also proceeds. In the first case it is obviously quite important to know what influence chlorine, entering into the hydrocarbon molecule, has upon introduction of the SO_2Cl group, and on the other hand, how the presence of the SO_2Cl group affects entry of chlorine, or of the second SO_2Cl group, into the molecule.

For elucidation of the first problem, the authors sulfochlorinated 1-chlorbutane. There resulted from the sulfochlorination a mixture of the chloranhydrides of chlorbutanesulfonic acids, from which it was difficult to isolate the individual isomers. To separate and to identify the resulting isomers, a method of thermal decomposition was investigated by the authors, and used. A mixture of butane dichlorides was obtained, which was converted into a mixture of disulfonychlorides (via the rhodanides), which was then separated by crystallization. There was isolated from 14.77 g of butanedisulfonylchloride mixture 3.45 g of the 1,4-isomer and 10.38 g of the 1,3-isomer, which were identified by their melting points. The first one had a m.p. of 83-84°, the second 40-41°. Isomers 1,1- and 1,2- were not found in noticeable quantities. Thus it is important to recognize that during the photochemical chlorination of chlorides, the entering SO_2Cl group is replaced by chlorine.

To investigate the effect of an SO_2Cl group upon entry of a second SO_2Cl group into the molecule, the chloranhydrides of butanesulfonic-1 and propanesulfonic-2 acids were photochemically sulfochlorinated. The sulfochlorides resulted from the corresponding chlorides by conversion to the rhodanides, with subsequent treatment of the latter by chlorine [2]. The chloranhydride of butanesulfonic-1-acid gave two dichloranhydrides: butanedisulfonic-1,4 and butanedisulfonic-1,3 acids. The chloranhydride of propanesulfonic-2 acid did not react with a mixture of chlorine and sulfur dioxide during six hours, with exposure to a mercury lamp. Thus, as with the chlorine atom, the SO_2Cl group also inhibit entry of a new SO_2Cl group into positions 1,1 and 1,2.

During the sulfochlorination of butanesulfonic-1 acid chloranhydride, there was separated, along with the dichloranhydrides, at this time, only two isomers: the chloranhydrides of 1-chlorbutanesulfonic-4 and 2-chlorbutanesulfonic-4 acid, i.e., the presence of the SO_2Cl group inhibits entry of the chlorine atom at the two carbon atoms nearest the SO_2Cl group. This deduction was also confirmed during the photochemical chlorination of butanesulfonic-1 acid chloranhydride, and in this case the chloranhydrides of 4-chlorbutanesulfonic-1 and 3-chlorbutanesulfonic-1 acid were obtained.

These simplest examples have indicated that during the photochemical processes, Cl and SO_2Cl, when present in the molecule, show a similar effect: they repel the second entering substituent (Cl or SO_2Cl); isomers 1,1 and 1,2 were not formed in noticeable quantities. Thus the chloranhydrides of sulfonic acids differ sharply from the haloanhydrides of the carboxylic acids. During chlorination of the chloranhydrides of butyric acid, the chloranhydride of α-chlorbutyric acid is formed, as was demonstrated by Markovnikov [3].

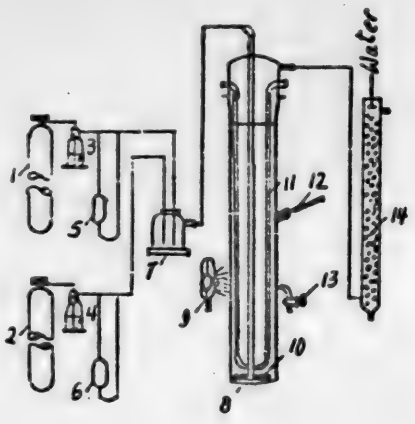
The bromination reaction of carboxylic acids in the presence of red phosphorous was studied in more detail by N. D. Zelinsky [4], through the formation of bromanhydrides. In this case bromine replaces the hydrogen atom at the α-carbon atom, even when the tertiary carbon atom is not in the α-position of the molecule. Thus, for example, α-bromisovaleric acid is formed from isovaleric acid, and from isocaproic acid is formed α-bromisocaproic acid. Upon chlorination of the free acids in the absence of phosphorous, this mechanism is not observed.

Thus, with chlorination of isovaleric acid in light, the β-chlorisovaleric acid [5] is formed, i.e., chlorine enters at the tertiary carbon atom, even though the latter is not in the α-position.

This peculiarity of the haloanhydrides of a carboxylic acid is explained by the fact that the latter, in distinction to the free acids, have a keto-enolic equilibrium shifted to the side of the enolic form. As is known, the sulfonic acids and their derivaties (but not the sulfones) have even less tendency to enolization than the carboxylic acids. To a certain degree this fact may serve as an explanation of the mechanism described above for the sulfochloride reaction.

EXPERIMENTAL

The reaction was carried out in Reactor 8 (see Figure) For gas feed the reactor was equipped with a tube ending in a porous plate. Temperature of the reaction mixture was controlled by thermometer 12, and was regulated by the supply of hot or of cold water in the U-shaped tube 11. Chlorine and sulfur dioxide were fed from tanks 1 and 2 through drying flasks 3 and 4 (filled with sulfuric acid) through mixer 7. The gas volumes were measured, respectively, by calibrated gasometers 5 and 6, illumination of the reaction mass being effected by a mercury lamp SVD Sh-250



Distance between the lamp and the reactor was 30 cm. The outgoing gases were absorbed in column 14 by water

Sulfochlorination of 1-Chlorbutane. Gaseous chlorine and sulfur dioxide were fed into 134.0 g of 1-chlorbutane (b.p. 77-78°; d_4^{20} 0.8869) for 7 hours, with exposure to a mercury lamp Chlorine was fed in at a rate of 1.1 ml/sec.; SO_2 at a rate of 2.2 ml/sec. At first the reaction mass became colored greenish yellow. After 30 minutes the mixture lost its color, and the temperature rose to 40°. After termination of the reaction, the mixture was flushed out with nitrogen. The increased weight after completion of the operation was 50.4 g. From a water bath 82.27 g of unreacted chlorbutane was distilled out from the reaction product. The residue was distilled in vacuo.

Fraction I, up to 70° (2.5 mm) 9.61 g. did not contain hydrolyzable chlorine and was not analyzed in detail (probably di- and poly-chlorbutanes).

Fraction II 105-110° (2.5 mm). 88 44 g.

Found %: Cl (sapon.) 18.51, 18 58. Cl (total) 37.16, 37.11. $C_4H_8O_2S_2Cl_2$. Calculated %: Cl (sapon.) 18.58; Cl (total) 37.17.

14 85 g of a mixture of dichlorbutanes resulted (b p. 130-155°) from 31.48 g of Fraction II, upon thermal decomposition 8.77 g of the dichlorbutanes was dissolved in 80 ml of ethyl alcohol, and to the solution was added 14.0 g of potassium rhodanide; the mixture was boiled for 40 hours on a water bath with a reflux condenser. After termination of reaction 300 ml of water was added to the mixture, the rhodanide separated and was extracted with ether. After removal of the ether, the rhodanide was suspended in water and treated with gaseous chlorine to the appearance of a yellow coloration, which indicated excess chlorine. The latter was blown off with nitrogen The chloranhydride formed separated in the form of a heavy, viscous oil, which solidified upon standing. The oil was extracted with ether, the ether solution was washed with water and dried with calcium chloride. After distilling off the ether 14 77 g of residue resulted. The latter was dissolved in 10 ml of benzene, and to the solution was added 20 ml of carbon tetrachloride 3 45 g of white needle crystals separated; after recrystallization from benzene and carbon tetrachloride, m p. was 83-84°.

Found %: Cl (sapon) 27.85, 27.77. $C_4H_8O_2S_2Cl_2$. Calculated %: Cl (sapon.) 27.84.

The crystals were identified as the chloranhydride of butanedisulfonic-1,4 acid from the melting point.

20 ml of petroleum ether was added to the filtrate resulting after separation of the chloranhydride of butanedisulfonic-1,4 acid. After standing, 10.38 g of white needle crystals separated out. After recrystallization from benzene and petroleum ether, m.p. was 40-41°.

Found %: Cl (sapon.) 27.80, 27.79. $C_4H_8O_4S_2Cl_2$. Calculated %: Cl (sapon.) 27.94.

The crystals were identified as the chloroanhydride of butanedisulfonic-1,3 acid from the melting point. Therefore Fraction II represented a mixture of two isomeri. chloroanhydrides of 1-chlorobutanesulfonic-4 and 1-chlorobutanesulfonic-3 acids in the ratio of 1:3, judging from the quantity of disulfonic acid chloroanhydrides formed.

Sulfochlorination of Propanesulfonic-2-acid Chloroanhydride. A mixture of gaseous chlorine and sulfur dioxide was passed into 10.0g of the chloroanhydride of propanesulfonic-2 acid for 6 hours, with exposure to a mercury lamp. Chlorine was passed in at the rate of 0.3 ml per sec, SO_2 at 0.6 ml per sec. At first the reaction mass was colored yellowish-green, and it did not decolorize for the duration of the reaction period. Weight of the reaction mass after blowing through with nitrogen was 38.2 g. The reaction product was fractionally distilled under vacuo and all of it distilled at 71-72° (13 mm); d_4^{20} 1.2652.

Found %: Cl (sapon.) 24.82, 24.88. $C_3H_7O_2SCl$. Calculated %: Cl (sapon.) 24.91.

Consequently, the chloroanhydride of propanesulfonic-2 acid remained unchanged.

Sulfochlorination of the Chloroanhydride of n-Butanesulfonic-1-acid. Gaseous chlorine and sulfur dioxide mixture was fed into 126.0 g of the chloroanhydride of butanesulfonic-1 acid for 10 hours with exposure to light. Chlorine was supplied at the rate of 0.83 ml/sec, SO_2 at 1.23 ml/sec. The yellow-green color that appeared at the start disappeared after 20 minutes. Reaction temperature was maintained at 30-35°. After blowing nitrogen through the reaction mass, the weight increase constituted 47.0 g. Upon heating the reaction product in an oil bath (100-120°) at 2 mm, 119.3 g was distilled off, residue remaining in the distilling flask being 50.8 g. The volatile portion was fractionally distilled.

Fraction I, 77-79° (8 mm) −31.4 g.
Found %: Cl (sapon.) 22.58, 22.63. $C_4H_9O_2SCl$. Calculated %: Cl (sapon.) 22.68.
Fraction II, 107-111° (8 mm) −79.5 g.
Found %: Cl (sapon.) 18.53, 18.52; Cl (total) 37.08, 37.11. $C_4H_9O_2SCl$. Calculated %: Cl (sapon.) 18.58; Cl (total) 37.17.

10.4 g of Fraction II was thermally decomposed. 4.79 g (yield 69.1%) of dichlorobutane mixture resulted.

Found %: Cl (total) 55.73, 55.81. $C_4H_8Cl_2$. Calculated %: Cl (total) 55.90.

3.0 g of dichlorobutanes was dissolved in 40 ml of alcohol, 7.0 g of potassium rhodanide was added and the mixture was boiled for 40 hours on a reflux. After addition of water, the rhodanide separated and was extracted with ether. After distilling off the ether, 20 ml of water was added to the remainder and the mixture was chlorinated. The aqueous emulsion was saturated with gaseous chlorine while stirring. The chloroanhydride formed was extracted with ether and dried with calcium chloride. After removal of the ether, 4.31 g of viscous oily liquid resulted, which did not solidify upon prolonged standing. The oil was dissolved in 5 ml of benzene and 10 ml of carbon tetrachloride was added to the solution. Upon standing, 0.32 g of white needle crystals separated, which were again recrystallized from benzene and carbon tetrachloride mixture, m.p. 83-84°. The sample mixed with the chloroanhydride of butanedisulfonic-1,4 acid did not show depression.

10 ml of petroleum ether was added to the filtrate from the preceding operation. Upon standing, 3.38 g of white needle crystals with m.p. 40-41° separated, A sample mixed with the chloroanhydride of butanedisulfonic-1,3 acid did not show depression of melting point. Consequently, Fraction II represented a mixture of the chloroanhyrides of 3-chlorobutanesulfonic-1 and 4-chlorobutanesulfonic-1 acids.

The residue from the distillation, which solidified to a brown crystalline mass, was dissolved in 50 ml of benzene and boiled with activated charcoal to decolorize. 100 ml of carbon tetrachloride was added to the filtrate. Upon standing, white needle crystals separated out (31.6 g). After repeated crystallizations, m.p. was 83-84°, which corresponded to the melting point of butanesulfonic-1,4 acid chloroanhydride. 100 ml of petroleum ether was added to the filtrate from the 1,4-isomer. Upon standing, 15.3 g of white needle crystals separated out with a m.p. of 40-40.5°, corresponding to the butanedisulfonic-1,3 acid chloroanhydride.

Chlorination of Butanesulfonic-1-acid Chloroanhydride. Chlorine was fed into 100.0 g of butanesulfonic-1 acid chloroanhydride, with exposure, for 8 hours, at the rate of 0.5 ml per sec. The reaction temperature was maintained at 30-35°. After blowing off with nitrogen, the increased reaction mass weight was 14.9 g. The product was fractionally distilled in vacuo:

Fraction I, b.p. 79-82° (9 mm) – 32.74 g; d_4^{20} 1.2069.
Found %: Cl (sapon.) 22.71, 22.68.
Fraction II, b.p. 100-112 (2 mm) – 81.4 g.
Found %: Cl (sapon.) 18.57, 18.63; Cl (total) 37.10, 37.24. $C_4H_8O_2SCl_2$. Calculated %: Cl (sapon.) 18.58; Cl (total) 37.17.

For determination of composition, 20.0 g of Fraction II was thermally decomposed. 9.20 g of isomeric dichlorobutanes resulted, boiling in the range 128-157° (754 mm). 8.4 g of dichlorobutanes obtained was converted into a mixture of dichloroanhydrides, proceeding as above. 11.8 g of dichloroanhydrides mixture resulted. From the mixture, by subsequent precipitation, first with carbon tetrachloride and then with petroleum ether, the following resulted:

a) 2.7 g of the chloroanhydride of butanedisulfonic-1,4-acid, m.p. 83.5°.
Found %: Cl (sapon.) 27.73, 27.78. $C_4H_8O_4S_2Cl_2$. Calculated %: Cl (sapon.) 27.84.

b) 7.8 g of the chloroanhydride of butanedisulfonic-1,3-acid, m.p. 39.5-40.5° Found %: Cl (sapon.) 27.81, 27.69. $C_4H_8O_4S_2Cl_2$. Calculated %: Cl (sapon.)27.84.

SUMMARY

The mechanism of Cl and SO_2Cl entry during the photochemical sulfochlorination reaction of hydrocarbon has been studied, as well as the influence of substituted groups already present in the molecule.

1-Chlorobutane, upon sulfochlorination, gave a mixture of isomeric chloroanhydrides of 4-chlorobutanesulfonic-1 and 3-chlorobutanesulfonic-1 acids in a ratio of approximately 3:1. Isomers 1,1 and 1,2 were not found.

During sulfochlorination of butanesulfonic-1 acid, the second SO_2Cl group enters only at position 4 and 3. Chlorination, which proceeds simultaneously, leads to exchange of the hydrogen atoms for chlorine in positions 4 and 3.

Under normal conditions of photochemical sulfochlorination, the chloroanhydride of propanesulfonic-2 acid remains unchanged.

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* See Consultants Bureau English translation, page. 209.

THE ESTERIFICATION MECHANISM OF GLUTARIC ACID

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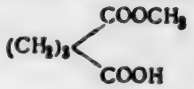
Only indirect methods are described in the literature for the synthesis of monomethylglutarate: by the method of methyl alcohol addition to the anhydride of glutaric acid [1], and as the result of acidolysis of dimethylglutarate with glutaric acid [2]. Attempts to synthesize monomethylglutarate by direct esterification of glutaric acid are as yet unknown. However, the following data are indicative of the feasibility of this method: 1) esterification conditions are close to acidolysis conditions; 2) the difference in hydrolysis constants for the glutaric acid carboxyls is quite significant ($K_1 = 0.1526$, $K_2 = 0.3940$).

Moreover, sebacic acid, the saponification constants of whose esters are approximately the same as for glutaric acid esters, according to the data of Adams [3], can be converted into the monomethyl ester by direct esterification. All of this, therefore, has preconditioned the attempted direct synthesis of monomethylglutarate by esterification of glutaric acid, avoiding intermediate stages.



Esterification experiments with glutaric acid, using various quantities of methanol in the presence of H_2SO_4, indicated that only dimethylglutarate is formed as the principal reaction product.

The effect of various solvents was also studied, among them those which differentiated the esterification course of glutaric acid. A mixture of 50 g of glutaric acid and 15 g of methanol (1:1) was dissolved in the appropriate solvent and heated on a water bath. The experimental results are summarized in Table 1.

TABLE 1

Expt. No.	Solvent	Quantity of H_2SO_4 (ml)	Duration of heating (hrs)	Yield of dimethyl-glutarate (%)	Yield of monomethyl-glutarate (%)
23	Acetone (125 ml)	5	1	31	–
24		5	4	26.6	13.6
25	Acetone (125 ml)	5	6	23.3	16.5
26		5	13	22.5	16.9
27	Dichloroethane (100 ml) . . .	–	13	20.0	–
28		5	13	36.6	–
29	Dichloroethane (50 ml +	–	13	16.6	–
30	acetone (50 ml)	5	13	41.6	12.7
31	Chloroform (100 ml)	–	13	16.0	–
33		5	13	55.0	–

Thus, esterifications of glutaric acid carried out in a medium of differentiating solvents, in the presence of catalyst (Experiments 23-26), and with their mixtures (Expt. 30), has resulted in the formation of small amounts of the acid ester. In the absence of catalyst, glutaric acid forms small amounts of the diester when in chloroform medium, and dichloroethane does not react at all in an acetone medium.

In order to improve reaction conditions, experiments were set up for the direct esterification of glutaric acid without catalyst (H_2SO_4).

TABLE 2

Expt. No.	Ratio of acid to alcohol quantities	Heating time	Yield	
			Mono- and dimethyl-glutarate (%)	Dimethyl-glutarate (%)
12	1:1	5	43.6	13.3
13	1:1.5	5	22.2	33.5
14	1:2	5	26.0	54.6
15	1:2.5	5	7.3	66.6
16	1:3	5	2.7	73.3
17	1:1	2.5	31.8	19.1
18	1:1	4.0	36.8	17.0
19	1:1	6.0	49.0	10.0
36	1:1	10.0	60.0	3.6
20	1:1	13.0	69.0	Traces
38	1:1	20.0	67.9	—

TABLE 3

Expt. No.	Diester and acid ratio (in moles)	Heating time (in hrs)	Quantity (in %)	
			Diester	Monoest
1	1:1	1.5	34.6	43.6
2	1:1	5.0	33.0	46.9
3	1:1	10.0	24.0	58.2
4	1:1	13.0	15.3	67.2
9	1:1	17.0	12.2	66.2

Preliminary experiments gave positive results immediately. Upon heating an equimolecular mixture of glutaric acid and methanol on an oil bath at 145-150° for 2 hours, a light-brown mass resulted, of sharp odor, containing 29.5% acid ester and 21.6% dimethylglutarate.

The experiments that followed clarified optimum reaction conditions, the most efficient ratio of initial substances—alcohol and glutaric acid, and also the relation of ester yields to reaction time. The results of these experiments are summarized in Table 2.

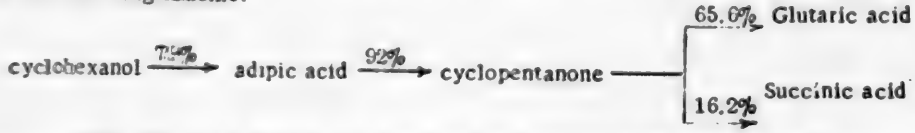
Consequently, direct esterification of glutaric acid by alcohol in the absence of H_2SO_4 catalyst leads to monomethylglutarate as the principal reaction product, while with an increase in the heating time of an equimolecular mixture, the acid ester yield is increased, and stabilizes after 13 hours of heating, while the content of dimethyl ester in the reaction mixture decreases. This brings to mind a thought that monomethylglutarate formation during the direct esterification of glutaric acid by alcohol is realized through an intermediate formation of dimethylglutarate, with its subsequent acidolysis by glutaric acid. To confirm this assumed formation mechanism for the glutaric acid ester, the authors carried out dimethylglutarate acidolysis experiments in relation to time. As a result of these experiments (Table 3) it was found that the most complete acidolysis occurs with equimolecular quantities of dimethylglutarate and glutaric acid. As experiments carried out under the same conditions as with esterification of glutaric acid were increased in time, the extent of acidolysis increased, and the dimethyl ester converted into monomethylglutarate, forming a mixture of unreacted diester and of monomethylglutarate after 13 hours heating.

Increase in experiment time to 17 hours has almost no effect upon the yield of monoester.

Thus, the experiments given in Table 3 confirm the authors' assumption concerning the fact that direct esterification of glutaric acid, as carried out by the authors, proceeds in two stages: the dimethyl ester formed during progress of the acid esterification enters into reaction with a second molecule of glutaric acid, forming monomethylglutarate.

EXPERIMENTAL

Glutaric Acid Synthesis. The glutaric acid was synthesized by a method developed by Markovnikov, with addition of precise specifications made by other scientists [4,5,6,1]. Synthesis was carried out according to the following scheme:



The mixture of glutaric and succinic acids resulting from oxidation of cyclopentanone was separated. In place of the orthodox, but complicated separation method for these acids by means of conversion to the barium salts, the authors utilized a sharp difference in solubility of glutaric and succinic acids in benzene.

1.42 kilograms of the acid, with m.p. 95-97°, resulted from 2.3 kilograms of cyclopentanone.

Esterification of Glutaric Acid. All experiments on esterification of glutaric acid and acidolysis of the dimethylglutarate were carried out in the same manner; a solvent and H_2SO_4 catalyst were added (Table 1) and the reaction mixture was heated in a round-bottomed flask with a reflux condenser on a boiling water bath. The glutaric acid esterification experiments without solvents, and the acidolysis, were carried out with heating to 145-150° on an oil bath. The reaction mass, heated through, was cooled and the flask contents were transferred to a Claison flask with fractionating column. After distilling off the solvent and alcohol, the residue on the water bath was fractionally distilled in vacuo. Fraction I, collected at 108-112° (23 mm), corresponded to dimethylglutarate. Fraction II, collected at 158-163° (23 mm) consisted principally of monomethylglutarate. Repeated fractional distillations of the ester fractions from several experiments indicated that Fraction 1 contained dimethylglutarate of sufficiently high purity.

The ester fraction (158-163°) was contaminated with 2-5% of glutaric acid, easily removable by repeated distillations in vacuo. Here the resulting product obtained boiled at 165-166° (23 mm).

d_{21} 1.1740; n_D^{21} 1.4419; MR_D 32.8908; calculated 33.0980.

SUMMARY

1. A method of monomethylglutarate synthesis has been developed by means of direct esterification of glutaric acid with methanol, in yields up to 69% of theoretical.

2. The effect of initial mixture composition, time of reaction, H_2SO_4 catalyst, and of solvents upon esterification of glutaric acid have been studied.

3. A reaction mechanism for monomethylglutarate formation by direct esterification of glutaric acid has been proposed. The reaction proceeds in two stages: at first dimethylglutarate is formed, which then, by acidolysis, is converted to the monomethyl ester of glutaric acid.

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COMPARATIVE HYDROGENATION OF UNSATURATED FATTY ACIDS C_{16}, C_{18} and C_{22}

P. A. Artamonov

As a development of the problem which was touched upon by the author in regard to the hydrogenation kinetics of unsaturated fatty acids [1,2], the author in the present investigation has undertaken the task of clarifying the effect of the carbon chain length upon the magnitude of the hydrogenation rate.

As objects for study, the unsaturated fatty acids, of general formulas $C_{16}H_{30}O_2$, $C_{18}H_{34}O_2$ and $C_{22}H_{42}O_2$, were selected, obtained partially by synthetic means, and partially by isolation from natural vegetable oils. Comparative hydrogenation experiments for the following pairs of unsaturated fatty acids were carried out: 1) hexadecene-2-acid-1 and octadecene-2-acid-1; 2) octadecene-2-acid-1 and docosene-2-acid-1; 3) octadecene-9-acid-1 and docosene-13-acid-1. Certain constants for these acids are given in Table 1.

TABLE 1

No.	Acid names	M	M.p.	Iodine No. according to Guble
1	Hexadecene-2-acid-1	254.24	49.0°	26.3•
2	Octadecene-2-acid-1	282.27	59.0	21.1•
3	Docosene-2-acid-1	338.34	68.5	18.75•
4	Octadecene-9-acid-1	282.27	14.2	89.3
5	Docosene-13-acid-1	338.34	33.5	74.38

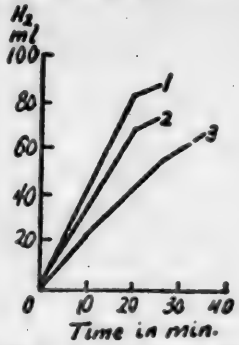

Fig. 1. 1) Hexadecene-2-acid-1; 2) octadecene-2-acid-1, 3) docosene-2-acid-1.

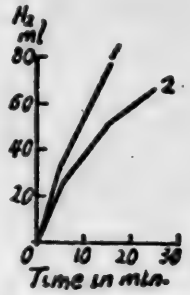

Fig. 2. 1) Octadecene-9-acid-1; 2) docosene-13-acid-1.

Hydrogenation was carried out with electrolytic hydrogen in dry diethyl ether at room temperature. Palladium black was used as a catalyst, obtained by the method of Willstätter. In the course of the experiments, the author used one and the same sample of catalyst and solvent in order to eliminate possible effects of the conditions of their preparation on the course of hydrogenation. For obtaining comparative data, hydrogenation was carried out on acid pairs. The experimental procedure was as follows: the investigated pairs of acids were placed together with the solvent into two glass containers (15 ml of an ester solution of the analyzed acids, 0.263 molar), set up in an apparatus for shaking, and connected with two burets filled with hydrogen such that each buret with container for hydrogenation constituted a closed cycle. The shaking device was set into movement by an electric motor. After defined time intervals, the hydrogen consumed was measured. The volume of absorbed hydrogen was brought to 0° and 760 mm pressure. The hydrogenation rate constant was calculated by an equation of zero order.

EXPERIMENTAL

1. Comparative Hydrogenation of Hexadecene-2-acid-1 and Octadecene-2-acid-1. The investigated acids were obtained by treatment of α-bromopalmitic acid and α-bromostearic acids with an alcoholic potassium hydroxide solution, using the methods described in the preceding works [1,3] by the author. Hydrogenation was carried out at a temperature of 22° and 760.5 mm. Experimental results of the hydrogenation are given in Table 2.

t = time (in minutes); v = volume of absorbed hydrogen (in milliliters), brought to 0° and 760 mm; dv = volume (in ml) of hydrogen absorbed within the time measured; k = quantity of hydrogen absorbed in one minute.

From the data of Table 2 it can be seen that hexadecene-2-acid-1 hydrogenates more rapidly than octadecene-2-acid-1. However, upon comparing the hydrogenation rates of octadecene-2-acid-1 and decosene-2-acid-1 (Table 3) it can be seen that octadecene-2-acid-1 in its turn hydrogenates more rapidly than decosene-2-acid-1.

• Lowered iodine numbers are characteristic for α- and β-unsaturated acids [3].

2. Comparative Hydrogenation of Octadecene-2-acid-1 and Docosenc-2-acid-1. The docosene-2-acid-1 necessary for the experiments was obtained by the author through a splitting off of the bromine from α-bromobehenic acid, using alcoholic alkali and heat [4]. The experimental results of hydrogenation are given in Table 3, and the course of the hydrogenation curves for the investigated acids is presented in Fig. 1.

TABLE 2

Hexadecene-2-acid-1				Octadecene-2-acid-1			
t	v	dv	k	t	v	dv	k
5	25	20	5.0	5	21.3	–	4.26
10	45	19.7	4.0	10	38.0	16.7	3.34
15	64.7	19.1	3.94	15	53.0	15.0	3.0
20	83.8	4.0	3.82	20	68.0	15.0	3.0
25	87.8	–	0.8	25	74.0	6.0	1.2

TABLE 3

Octadecene-2-acid-1				Docosene-2-acid-1			
t	v	dv	k	t	v	dv	k
5	21.4	17.0	4.28	5	14.0	–	2.80
10	38.4	16.4	3.4	10	25.5	11.5	2.30
15	54.8	16	3.28	15	35.5	10.0	2.00
20	70.4	4.5	3.20	20	44.75	9.25	1.85
25	75.3	–	0.9	25	53.75	9.0	1.85
–	–	–	–	30	60.75	7.0	1.40
–	–	–	–	35	66.25	55.	1.10

TABLE 4

Octadecene-9-acid-1				Docosene-13-acid-1			
t	v	dv	k	t	v	dv	k
5	35	–	7.0	5	25.0	–	5.0
10	55.5	20.5	4.1	10	38.0	13.0	2.6
15	75.5	20.0	4.0	15	50.0	12.0	2.4
20	76.35	0.85	0.17	20	59.0	9.0	1.8
25	–	–	–	25	67.0	8.0	1.6
30	–	–	–	30	–	–	–

Analysis of the resulting data (Tables 2, 3 and Fig.1) indicates that the size of the fatty acid molecule evidently affects the hydrogenation course, namely, the longer the carbon chain length for the unsaturated fatty acid molecule, the slower the addition of hydrogen at the double bond proceeds.

Of the three acids investigated by the author, docosene-2-acid-1, with 22 carbon atoms in its molecule (M = 338.34), hydrogenates the slowest, and hexadecene-2-acid-1 with 16 carbon atoms in its molecule (M = 254.24) hydrogenates the fastest.

3. Comparative Hydrogenation of Octadecene-9-acid-1 and Docosene-13-acid-1. Of interest to the author was the problem: is the above-mentioned mechanism preserved between the unsaturated fatty acid molecular weight and its hydrogenation rate if fatty acids with different double bond positions from the carboxyl group are taken, than the α-unsaturated acids which were taken for investigation by the author. To solve this problem, a comparative hydrogenation of octadecene-9-acid-1 (oleic acid) and docosene-13-acid-1 (erucic acid) was carried out. The acids necessary for the experiments were isolated from natural vegetable oils. Oleic acid was isolated from olive oil, and erucic from rape oil. Conditions of hydrogenation were the same as in the preceding cases. Experimental results are given in Table 4 and in Fig. 2.

It can be seen that here too is maintained the relation observed by the author between the unsaturated fatty acid molecular weight and its hydrogenation rate, namely: the longer the carbon chain length of the molecule, the slower does hydrogenation proceed. Docosene-13-acid-1 (erucic acid) hydrogenates considerably slower (1.5-2 times) than does octadecene-9-acid-1 (oleic acid). From this it is possible to explain the fact which is met everyday in practice that oils from the cruciferae family (rape, mustard and colza), which contain large amounts (up to 50%) of erucic acid, hydrogenate considerably slower, as a rule, than sunflower, cotton and other oils, which are composed principally of the triglycerides of the unsaturated fatty acids C_{18} and C_{18}.

It is of interest to note that the rate of hydrogen addition to the double bond of an unsaturated fatty acid apparently depends, to a more considerable extent upon the carbon chain length of the molecule, than upon the carboxyl group position with respect to the double bond.

In the author's preceding work on a study of the hydrogenation rate of octadecene acids [1], it was established that as the double bond becomes farther removed from the carboxyl group, the rate of hydrogen addition to the double bond increases. Proceeding from this position, erucic acid, in which the double bond is in position 13-14 from the carboxyl group, should hydrogenate at a greater rate than oleic, whose double bond in the chain is considerably nearer (9-10) to the carboxyl group. However, as can be seen, the results

are contrary, due to a higher molecular weight of erucic acid as compared with oleic acid. Consequently, the mechanism of hydrogen addition rate to unsaturated fatty acids in relation to the double bond position is apparently preserved only for acids of the same order.

SUMMARY

1. The rate of hydrogenation of unsaturated fatty acids decreases with an increase in molecular weight. Hexadecene-2-acid-1 hydrogenates more rapidly than octadecene-2-acid-1, and in its turn octadecene-2-acid-1 hydrogenates at a more rapid rate than docosene-2-acid-1.

2. The difficulty in hydrogenation of vegetable oils from the cruciferrae family (rape, mustard, and colza) which is encountered in practice is explained by the low hydrogenation rate of docosene-13-acid-1 (erucic acid) as compared with the hydrogenation rates of hexadecene and octadecene acids which enter into the composition of sunflower, cotton and other oils.

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* See Consultants Bureau translation, p. 1187.
** See Consultants Bureau translation, p. 2037.
*** See Consultants Bureau translation, p. 2041.

ALKYL ESTERS OF GLYCEROL

M. S. Malinovsky and V. M. Vvedensky

The present investigation was undertaken with the purpose of clarifying the influence of alcohol type upon its order of addition to glycides and the yield of glycerol monoester.

Methyl, ethyl, propyl, iso-propyl, n-butyl, iso-butyl, ter-butyl, n-amyl, iso-amyl, allyl and benzyl alcohols were taken. All of the alcohols mentioned form monoesters (some of them synthesized for the first time by the authors), and at the same time the following regularities were observed.

1) The normal primary alcohols give the highest yields (approximately 60-80%) of glycerol monoesters 2) Primary alcohols of iso-structure form monoesters in poorer yields than the normal alcohols. Thus, for example, the monoester yield for isobutyl alcohol was 29%, and for isoamyl 34%. 3) The secondary alcohols give monoesters, but not with such high yields, on the average 30-35%. 4) Tertiary alcohols, as was expected, gave the monoesters in poor yields (3-4%), and prolonged heating of their components is required, up to approximately 20 hours. 5) Benzyl alcohol reacts with glycide with more difficulty than with the secondary alcohols, and the monoester yield reaches 16-18%.

None of the synthesized glycerol esters mix with benzene, and apart from the methyl ester, they are insoluble in water. They mix with ethyl alcohol and acetone in all proportions. Monoesters with amyl, iso-amyl and allyl radicals are insoluble in ethyl ether. The boiling points and specific gravities of the monoesters are given in the Table.

In the reaction of alcohol with a glycide the formation of an α- or a β-form of the monoesters may be expected. The authors obtained only α-esters, identical in structure with the esters resulting from the α-chlorohydrin of glycerol and the alcoholates of the corresponding alcohols. Due to the fact that some of the glycerol monoesters described here have been synthesized for the first time by the authors, it was obligatory, for structure confirmation, to synthesize them from the alcoholates by the procedure indicated above; the esters in this case resulted in poor yields. Conformity of the ester constant synthesized from the glycide and the α-chlorohydrin of glycerol indicated that only the α-monoesters of glycerol result from glycides and alcohols.

The results obtained by the authors are in good agreement with the data of A. A. Petrov and M. G. Vladimirova [1]. The authors mentioned established that for the most part only α,γ-diesters are formed, i.e., that the oxide ring of glycide is open on the side of the tertiary carbon atom, which has likewise been observed by the present authors.

EXPERIMENTAL

Condensation of Glycide with Methyl Alcohol. Taken: 7.5 g (0.1 mole) of glycide, 16 g (0.5 mole) of methyl alcohol, and 1% of the mixture weight in concentrated sulfuric acid in the role of catalyst.

Sulfuric acid was added to the alcohol with cooling, and then the glycide in small portions. With such a mixing order for the components, the highest yield of the monoester resulted. If one proceeds, on the contrary, to mix alcohol with the glycide and then to add the acid, then each drop of the latter reacts very rapidly. The glycide oxide resinifies. Under the conditions indicated above, resinification was not observed, although the reaction proceeded with strong heat evolution, because of which the flask had to be well-cooled.

After termination of reaction, the sulfuric acid was neutralized with barium carbonate and the ether was distilled off in vacuo. 7.9 g of monoester resulted, which constituted 75%.

Repeated experiments have indicated that a two-fold or three-fold decrease in quantity of alcohol always decreases the monoester yield by 50%. A 0.1% decrease in quantity of acid also decreases the ester yield to a high degree: on the other hand, an increase in quantity of acid up to 2% increases the monoester yield up to 85%.

A further increase in the quantity of acid did not affect the ester yield.

TABLE

The Properties of Glycerol Monoesters

No.	Name of Ester	Formula	B.p. (731-736 mm)	d^{20}	Per cent OH groups	
					found	calculated
1	α-Methyl ester of glycerol[2]	$CH_3OCH_2CH(OH)CH_2OH$	198-200°	1.183	—	—
2	α-Ethyl ester of glycerol [3]	$C_2H_5OCH_2CH(OH)CH_2OH$	219-222	1.0947	—	—
3	α-Propyl ester of glycerol [4]	$C_3H_7OCH_2CH(OH)CH_2OH$	221-224	1.0826	—	—
4	α-Isopropyl ester of glycerol	$(CH_3)_2CHOCH_2CH(OH)CH_2OH$	187-190	1.0063	25.10	25.35
5	α-Butyl ester of glycerol	$C_4H_9OCH_2CH(OH)CH_2OH$	226-227	1.0585	22.65	22.95
6	α-Isobutyl ester of glycerol	$(CH_3)_2CHCH_2OCH_2CH(OH)CH_2OH$	216-218	1.0656	22.21	22.95
7	α-Ter-Butyl ester of glycerol	$(CH_3)_3COCH_2CH(OH)CH_2OH$	209-211	1.0764	22.40	22.95
8	α-Amyl ester of glycerol [5]	$C_5H_{11}OCH_2CH(OH)CH_2OH$	257-260	1.0663	—	—
9	α-Isoamyl ester of glycerol	$(CH_3)_2CHCH_2CH_2OCH_2CH(OH)CH_2OH$	248-250	1.0047	—	—
10	α-Ailyl ester of glycerol	$H_2C=CHCH_2OCH_2CH(OH)CH_2OH$	209-210	1.0869	25.54	25.74
11	α-Benzyl ester of glycerol	$C_6H_5CH_2OCH_2CH(OH)CH_2OH$	274-276	1.0263	18.60	18.72

The ester which the authors have synthesized for the first time from glycide was obtained by heating sodium methylate with the α-chlorohydrin of glycerol [2].

The remaining esters given in the Table were synthesized in the same manner as the methyl ester, except that in certain instances the reaction mixture had to be heated on a water bath. In a majority of the cases, 2 hours of heating was quite adequate for maximum ester yield, and it was only the condensation of glycide with ter-butyl alcohol that required 20 hours of heating.

0.1 mole of glycide, 0.5 mole of the corresponding alcohol and sulfuric acid to the amount of 2% of the mixture weight were taken in all condensations.

The molecular weights of the synthesized esters were determined and the deviation between found and calculated data consisted of 1 to 3% for the hydroxyl group content.

The esters indicated in the Table under Nos. 5, 8 and 10 were obtained, moreover, from the glycerol α-chlorohydrin by the method given in the literature.

SUMMARY

1. The condensation of glycide with various primary, secondary and tertiary alcohols has been investigated.

2. The mechanism of glycerol monoester formation from glycide and conditions for highest yields have been brought out.

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INVESTIGATION OF OLEFIN OXIDES

CONDENSATION OF OLEFIN OXIDES WITH PHOSGENE

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As is known, the chloroanhydride of carbonic acid, or phosgene, reacts readily with alcohols to form esters of chlorocarbonic acid. A second phosgene chlorine atom enters into reaction with excess alcohol and high temperature, which leads to the complete esterification of carbonic acid. In order to avoid this second reaction, strong cooling and considerable phosgene excess in relation to alcohol are necessary, which leads to variations in this reaction, namely: the alcohol can be reacted with liquid phosgene with strong cooling [1], or the alcohol can be dropped onto charcoal fragments saturated with phosgene [2].

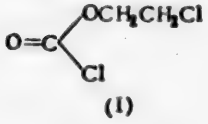
When phosgene and alcohol react, hydrogen chloride is usually evolved, which, upon dissolving in the liquid, shifts the equilibrium (for the first reaction) to the left, leading to decreased yields of chlorocarbonic esters. To avoid this reverse reaction, hydrogen chloride must be removed from the reaction medium, which is realized either by bubbling air through, or by addition of weak organic bases [3] (dimethylaniline, pyridine, antipyrine, and others), or by addition of marble. In the latter case water must also be introduced for solution of the calcium chloride which results from the reaction process.

Quite obviously the thought arose of carrying out the first reaction in such a manner as to have no worry concerning the formation of a full ester of carbonic acid, or the reverse process, which leads to decomposition of chlorocarbonic esters. For this purpose the authors made use of olefin oxides, which when reacted with phosgene should be completely added to the latter, as the result of which the need for fixing hydrogen chloride no longer arises.

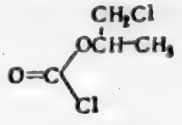
During the reaction of phosgene with olefin oxides, chlorocarbonic esters or the full esters of carbonic acid may be expected.

In reality it was found that reaction proceeds in the first direction, and even with a large excess of oxide the full ester of carbonic acid does not result. This was also confirmed by special experiments on the condensation of the readily-prepared ester of chlorocarbonic acid $CH_3O-C(=O)-Cl$ with ethylene, propylene and epichlorhydrin oxides. Despite the fact that the oxide was passed into (or was added dropwise to) the above-indicated ester, which was heated on a water bath, condensation was not observed, and the ester remained unchanged.

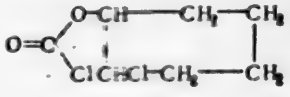
The authors synthesized the following esters of chlorocarbonic acid from the olefin oxides:



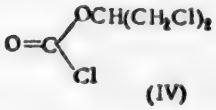
(I)



(II)



(III)



(IV)

The structure of these esters was confirmed by saponification, the result of which gave the corresponding chlorohydrins of the glycol. Furthermore, some of the above-mentioned esters are described in the literature (synthesized by other methods), and their constants coincide fully.

According to their odor, the chlorocarbonic acid esters are similar to the methyl ester of chlorocarbonic acid.

EXPERIMENTAL

Phosgene was obtained from carbon tetrachloride by reacting with oleum of high percentage [4].

The esters were synthesized as follows. The calculated quantity of cooled olefin oxide was slowly added to a solution of the determined quantity of phosgene in ethyl bromide. The reaction proceeded violently, and so the mixture was cooled with water and ice for the entire period. After introduction of the oxide the reaction mixture was left to stand overnight at 0°, and the solvent was then distilled off, the residue washed with ice water, dried with anhydrous sodium sulfate and redistilled

An excess of phosgene does not impair the reaction, and it is better to take somewhat more of the latter than of olefin oxide. As solvents, benzene, toluene, carbon tetrachloride, dichloroethane, and others, may be taken, but best of all is ethyl bromide. The ethyl bromide has a low boiling point (+ 38°), and consequently is easily removable from the resulting chlorocarbonic acid ester and does not contaminate the latter. The other indicated solvent always contaminate the resulting chlorocarbonic ester and for its purification repeated distillations are required.

β-Chloroethyl Ester of Chlorocarbonic Acid (I). This product resulted in 50% yield from ethylene oxide and phosgene, and is a colorless liquid, b.p. 153°.

d_4^{18} 1.3760. Found %: Cl 50.08. $C_3H_4O_2Cl_2$. Calculated %: Cl 49.65.

This ester is described in the literature and was synthesized for the first time by the action of chlorine upon chlorcarbonic acid ethyl ester [5] together with the α-isomer, and also from ethylenechlorhydrin and phosgene [6]. According to the literature data, the ester has a b.p. of 152,5° and d_4^{20} 1.3825.

β-Chloroisopropylester of Chlorocarbonic Acid (II). This ester was obtained from propylene oxide and phosgene in 55% yield. A colorless liquid with b.p. 68-70° at 70 mm.

d_4^{18} 1.1610; n_D^{18} 1.44619.

0.2080 g substance: 0.3784 g AgCl. Found %: Cl 45.00. $C_4H_6O_2Cl_2$. Calculated %: Cl 45.22.

Upon heating the ester with an aqueous solution of potash, propylenechlorohydrin resulted, the presence of which confirms the written formula.

o-Chlorocyclohexyl Ester of Chlorocarbonic Acid (III). This ester resulted in 75-80% yield from cyclohexene oxide. A colorless liquid with b.p. 108-110° at 13 mm.

d^{18} 1.2158. 0.1938 g substance: 0.2798 g AgCl. Found %: Cl 35.73. $C_7H_{10}O_2Cl_2$. Calculated %: Cl 36.0

When the ester was heated with an aqueous solution of potash, cyclohexene chlorohydrin resulted, which confirms the proposed formula.

β,β'-Dichloroisopropyl Ester of Chlorocarbonic Acid (IV). This ester resulted in 80% yield from epichlorohydrin and phosgene. B.p. 78-80° at 20 mm.

d^{20} 1.3736; n_D^{20} 1.4804.

0.1928 g substance: 0.4304 g AgCl. Found %: Cl 55.02. $C_4H_5O_2Cl_3$. Calculated %: Cl 55.61.

The ester is described in the literature; it was obtained from symmetrical dichloroisopropyl alcohol and phosgene [7].

SUMMARY

1. The chlorosubstituted chlorocarbonic esters may be synthesized successfully by reaction of phosgene with the corresponding olefin oxides.

2. The intermediate chlorinated esters of carbonic acid do not result from an interaction of phosgene and olefin oxides, which simplifies the purification of chlorinated esters of chlorocarbonic acid.

3. It is most expedient to condense the olefin oxide with phosgene in ethyl bromide solution which is readily removed and does not contaminate the principal reaction product.

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THE AMIDATION MECHANISM OF CARBOXYLIC ACIDS BY AMIDES OF SULFURIC ACID

A. V. Kirsanov

At the present time enough factual material has been accumulated to evaluate possible amidation mechanisms of carboxylic acids by sulfuric acid amides and to verify them experimentally. Acid amides [1] result during the sulfamide reaction with carboxylic acids, and with dimethylsulfamide only the acid dimethylamides result [2]:

$$RCOOH + NH_2SO_2NH_2 \rightarrow RCONH_2 + NH_2SO_3OH;$$

$$RCOOH + NH_2SO_2N(CH_3)_2 \rightarrow RCON(CH_3)_2 + NH_2SO_3OH.$$

Upon reacting diphenylsulfamide with carboxylic acids, the phenylamides of carboxylic acid result [3]:

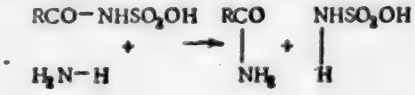
$$RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow RCONHC_6H_5 + C_6H_5NHSO_3OH.$$

All of these reactions can be very well explained if an amidation mechanism similar to the esterification mechanism described in one of our preceding works [1] is adopted. According to this mechanism, the presence of "free" hydrogen in sulfamide is not essential, and amidation should also proceed for quaternary substituted sulfamides. However, it was determined that carboxylic acids do not react with quaternary substituted sulfamides. Consequently, the amidation mechanism proposed earlier is also inaccurate.

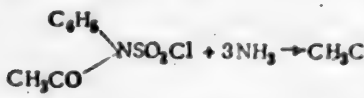
Evidently one or two "free" hydrogen atoms in the sulfamide molecule are indispensable for the amidation reaction. It was found that the interaction of trisubstituted sulfamides with carboxylic acids proceeds readily, while in the case of asymmetrical dimethylphenylsulfamide, a mixture of dimethylamides and phenylamides results:

$$RCOOH + (CH_3)_2NSO_2NHC_6H_5 \rightarrow \underset{\sim 55\%}{RCON(CH_3)_2} \text{ and } \underset{\sim 30\%}{RCONHC_6H_5}.$$

Inasmuch as only one "free" hydrogen in the sulfamide is necessary and sufficient, it was therefore thought that the intermediate products were the acylsulfamides of acylamino acids ($RCONHSO_2NH_2$ or $RCONHSO_2OH$) which are further aminolyzed by ammonia or amines at the CN bond with amide and sulfamino acid formation:



Aminolysis may proceed both intramolecularly and extramolecularly. The likelihood of such aminolysis is confirmed by the fact that during reaction of ammonia or amines with the chloranhydrides of aryl-acylsulfamino acids, there occurs an analogous reaction [4]:



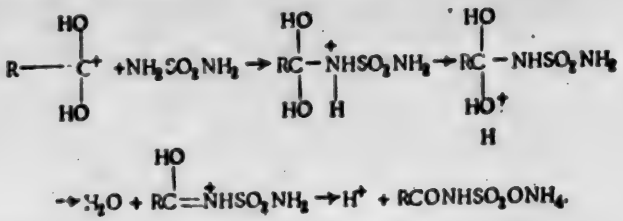
The hypothesis of N-S bond hydrolysis is eliminated because if this hypothesis were true, then the carboxylic acid dimethylamides could not result from amidation by asymmetrical dimethylsulfamides. For the same reasons, sulfamic acid ($N{\equiv}SOOH$) and isosulfanic acid ($NH{=}SO_2$) could not become active amidating agents. But isosulfanic acid may become a passive amidating agent, i.e., by removing water from ammonium or substituted ammonium salt.

This hypothesis seems to be somewhat artificial, but has not as yet been refuted experimentally. However, from the hypothesis we cannot draw the conclusions that were infefred (and experimentally confirmed) from the theory which assumes that the acyl sulfoaminic acids are formed as intermediate products.

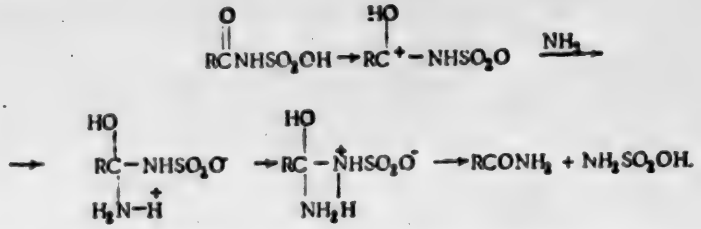
The formation of acylsulfaminic acids can occur through two mechanisms: isosulfanic acid is formed as an intermediate product:

$$(CH_3)_2NSO_2NHC_6H_5 + C_6H_5N{=}SO_3 \xrightarrow{RCOOH} RCON(C_6H_5)SO_2OH,$$

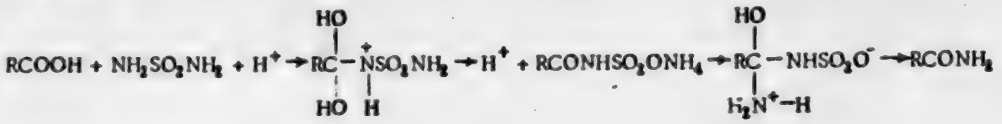
or, which is more probable, according to the mechanism which is similar to the esterification mechanism, but somewhat different from that earlier proposed [1], i.e., according to the scheme:



Aminolysis may proceed by the same scheme, i.e.:



Thus it is quite probable that amidation of carboxylic acid by sulfamides proceeds according to the following mechanism:



This mechanism explains all of the observed facts except one. If the proposed mechanism is correct, then only dimethylamide should result during interaction of dimethylphenylsulfamide with the carboxylic acid, whereas in actuality a mixture of both dimethylamides and phenylamides results. This nonconformity is explained by the fact that upon reacting the carboxylic acids with unsubstituted or asymmetric di-substituted sulfamide, sulfaminic acid is formed as a stable, highly difficult to hydrolyze, sulfaminic acid, and the reaction of carboxylic acids with dimethylphenylsulfamide results in an unstable side product, phenylsulfaminic acid, which is extremely easy to hydrolyze. This acid is well known in the form of salts, but no one as yet has apparently isolated it in the pure state. Buhner gives a m.p. above 280° for the phenylsulfaminic acid, and Wohl and Koch report that phenylsulfaminic acid melts at 77° [5]. A characteristic property of phenylsulfaminic acid is found to be the tendency for hydrolysis of the N-S bond; consequently it might be assumed that phenylsulfamic acid would be acidolyzed by carboxylic acids, with the formation of carboxylic acid phenylamides: $C_6H_5NHSO_2OH + RCOOH \rightarrow RCONHC_6H_5 + H_2SO_4$. This hypothesis was tested and experimentally confirmed.

The ammonium salt of phenylsulfamino acid was obtained by reacting sulfamino acid with aniline [6], and without purification was heated with p-nitrobenzoic acid in pyridine solution. From this the corresponding phenylamide resulted with a yield about 30% of theory. Thus the accuracy of the theoretical assumption was confirmed, and one more way of directly transforming carboxylic acids into the phenylamides has been found. It is possible that it will find practical application, since the arylsulfaminic acids in the form of their ammonium salts are cheap and easily accessible.

Formation of phenylamides from the phenylsulfoaminic acid and carboxylic acids was again confirmed by an additional experiment. A mixture of 2 moles of p-nitrobenzoic acid was heated in pyridine solution with 1 mole of phenylsulfamide. p-Nitrobenzanilide resulted in 73.6% yield by the following scheme:

$$2RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow 2RCONHC_6H_5 + H_2SO_4,$$

and in a yield of 147.2% of theory based upon calculation according to the scheme

$$RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow RCONHC_6H_5 + C_6H_5NHSO_2OH.$$

This can only be explained by the fact of phenylsulfaminic acid acidolysis by the carboxylic acid, with formation of the phenylamide. Unsubstituted sulfaminic acid and alkylsulfaminic acids do not react, under similar conditions, with carboxylic acids. Thus the proposed amidation mechanism fully explains all of the known facts. But theory

should not only explain, it should also predict. Thus, the second stage of the reaction is found to be aminolysis of acylsulfoaminic acid according to the scheme:

$$\begin{matrix} RCO-NHSO_2OH \\ + \\ H_2N-H \end{matrix} \longrightarrow RCONH_2 + NH_2SO_2OH.$$

Therefore, the first deduction is: If the amidation reaction is carried out with an unsubstituted sulfamide in the presence of an "auxiliary" amine, then a substituted amine should result, for example:

$$RCOOH + NH_2SO_2NH_2 \rightarrow RCONHSO_2ONH_4;$$

$$RCONHSO_2ONH_4 + C_6H_5NH_2 \rightarrow RCONHC_6H_5 + NH_2SO_2ONH_4.$$

This deduction was confirmed in the case of sulfamide-p-nitrobenzoic acid-aniline. Calculated on the basis of p-nitrobenzoic acid which entered into reaction, there was obtained: phenylamide, 58% of theoretical, unsubstituted amide – about 36% of the theoretical.

Production of the phenylamide may also be explained by the fact that the aniline reacts with sulfamide to give phenylsulfamide and diphenylsulfamide, which then phenylamidates the acid:

$$NH_2SO_2NH_2 \xrightarrow{C_6H_5NH_2} C_6H_5NHSO_2NH_2 \xrightarrow{C_6H_5NH_2} C_6H_5NHSO_2NHC_6H_5;$$

$$2RCOOH + C_6H_5NHSO_2NHC_6H_5 \rightarrow 2RCONHC_6H_5 + H_2SO_4.$$

Experiment (see experimental portion [7]) has shown that the reaction indeed does also proceed in this direction, but even under conditions considerably more favorable for sulfamide phenylation, only 14% diphenylamide is formed and can only produce at the utmost about 21% of phenylamide. However, in actuality this quantity is much smaller, since the rate of reaction of acid with sulfamide is much higher than the sulfamide reaction rate with aniline. Hence if follows that the main bulk of phenylamide is formed at the expense of phenylaminolysis of acylsulfaminic acid.

Moreover, the phenylamide formation can be explained by a reamidation of unsubstituted amide during reaction with aniline. Specially arranged experiments indicated that under the specified conditions reaction does not proceed significantly.

Second deduction: During reaction with prepared acylsulfaminic acids of ammonia (or of amines) the amides (or substituted amides) of the carboxylic acids and of sulfaminic acid should result:

$$RCONHSO_2OH + C_6H_5NH_2 \rightarrow RCONHC_6H_5 + NH_2SO_2OH.$$

This hypothesis was experimentally verified by heating benzamide and betainopyridinium-sulfaminic acid mixture [8] to obtain the pyridine salt of benzoyl sulfaminic acid. The reaction mixture (without isolation of the benzoylsulfaminic acid) was heated with aniline. About 70% of the theoretical quantity of benzanilide (calculating on the basis of benzamide entering into reaction) was isolated. It follows that the second deduction is also experimentally confirmed.

Thus the proposed theory for the amidation mechanism of carboxylic acids by sulfamides not only confirmed all known experimental data, but also gave an opportunity for predicting two new reactions; therefore there are grounds to believe that the proposed mechanism is correct.

EXPERIMENTAL

Interaction of Tetrasubstituted Sulfamides with Carboxylic Acids. Acetic and benzoic acids, symmetrical dimethyldiphenylsulfamide [7], diethyldiphenylsulfamide and tetramethylsulfamide [9] were selected as the experimental compounds. Six experiments in all were carried out, of which one is described in detail, namely the interaction of benzoic acid and dimethyldiphenylsulfamide.

0.01 mole of dimethyldiphenylsulfamide (2.76 g), 0.01 mole of benzoic acid (1.22 g) and 5.0 ml of dry pyridine mixture were heated for 4 hours with a reflux condenser on an oil bath at 116°. The reaction mixture remained transparent, and the yellowing was hardly noticeable. The pyridine was distilled off in vacuo, the crystalline residue was treated with 15 ml of 1 0 N caustic soda solution, and then with 100 and with 50 ml of ether. The ether solution was dried with Na_2SO_4, and the ether was distilled off. The crystalline residue was dried over H_2SO_4 in vacuo of 0.5 mm for 24 hours and represented pure dimethyldiphenylsulfamide. Yield was 2.74 g (99.2% of the quantity taken), m.p. 95.5-97.0°, a sample mixed with known dimethyldiphenylsulfamide melted at 96.0-97.0° (uncorrected).

The alkaline solution was acidified with 10.0 ml of 2.0 N hydrochloric acid, and the benzoic acid was extracted with ether. The ether solution was dried with Na_2SO_4, the ether distilled off, and the residue dried over H_2SO_4 in vacuo of 0.5 mm. The yield of benzoic acid was 1.20 g (98.2% of the quantity taken), m.p. 119-120°, a sample mixed with known benzoic acid melting at 119.5-121°.

The remaining five experiments were carried out under the same conditions. In all cases the tetrasubsituted sulfamides were recovered in quantities amounting to 99.1-99.4% of the original, benzoic acid in quantities of 97.8-98.5% of original. Acetic acid was not separated.

Reaction of Dimethylphenylsulfamide with Benzoic Acid. 0.01 mole of dimethylphenylsulfamide (2.0 g), 0.01 mole of benzoic acid (1.22 g) and 5.0 ml of dry pyridine were heated for 3 hours on an oil bath at 115°. The pyridine was distilled off in vacuo and the residue was treated with 150.0 ml of ether and 10 ml of 2.0 N HCl. After vigorous shaking, the ether solution was separated, washed three times with 1.0 ml portions of water, then with 15 ml of 1.0 N caustic soda solution, dried with Na_2SO_4 and evaporated to dryness. The residue consisted of 1.42 g of benzanilide and benzdimethylamide mixture. For separation, the mixture of amides was treated with 30 ml of petroleum ether (b.p. 85-95°) in which the benzdimethylamide is very readily soluble, and the undissolved benzanilide was filtered off with suction and washed 3 times with 1.0 ml portions of petroleum ether. Yield 0.65 g (33.0% of theoretical). After recrystallization from alcohol, large lustrous flakes resulted, m.p. 161-162° (uncorrected), which did not give depression with authentic benzanilide.

The filtrate was treated with 0.1 g of activated charcoal and evaporated in vacuo. The resulting colorless oil, upon addition of benzdimethylamide seeder crystallized immediately to a completely dry, crystalline mass. Yield was 0.75 g (50.2% of the theoretical), m.p. 39-41° (uncorrected), which did not give depression with an authentic sample of benzdimethylamide.

Reaction of Dimethylphenylsulfamide with p-Nitrobenzoic Acid. 0.01 mole of dimethylphenylsulfamide (2.0 g), 0.01 mole of p-nitrobenzoic acid (1.76 g) and 5.0 ml of pyridine mixture were heated for 3 hours on an oil bath at 115°. After distilling off the pyridine in vacuo, 10.0 ml of 1.0 N caustic soda solution and 40.0 ml of water were added to the residue. After 20 minutes, the fine, crystalline precipitate was filtered off with suction and washed 4 times with 5.0 ml portions of water. The precipitate (0.99 g) consisted principally of p-nitrobenzoic acid phenylamide, but also contained a certain amount of dimethylamide. A considerable quantity of dimethylamide was present in the aqueous filtrate which was extracted three times with 5 ml portions of ether. The ether solution was dried with Na_2SO_4 and the ether distilled off. The residue was dried in vacuo over sulfuric acid. After drying, 0.93 g of crude dimethylamide of p-nitrobenzoic acid resulted.

The phenylamide and the dimethylamide were separated by the use of petroleum ether (b.p. 85-95°).

The mixture of amides (0.99 g) was boiled with 75 ml of petroleum ether, the undissolved phenylamide removed by suction at the boiling point and washed 3 times with 5 ml portions of boiling petroleum ether. 0.70 g (28.9% theoretical) of p-nitrobenzoic acid phenylamide resulted, in the form of a dirty-gray, fine crystalline powder with m.p. 208-210°. After recrystallization from 15 ml of butanol, the phenylamide resulted in the form of almost colorless, large, flat needles with m.p. 210-211° (uncorrected), which did not give a depression with known p-nitrobenzanilide.

To remove the phenylamide from the petroleum ether solution, 0.2 g of activated charcoal was added to the solution, cooled to 75°, and filtered at the same temperature. After cooling, the p-nitrobenzoic acid crystals crystallized out in the form of thin, colorless needles.

The crude dimethylamide (0.98 g) was also crystallized from 75 ml of boiling petroleum ether with addition of 0.2 g of activated charcoal and filtration at 75°. The total yield of dimethylamide was 1.20 g, i.e., 61.9% of the theoretical quantity, m.p. 93-95° (uncorrected), which did not give depression with authentic p-nitrobenzoic acid dimethylamide.

Synthesis of the Phenylsulfaminic Acid Ammonium Salt. 0.2 mole of freshly distilled aniline (18.6 g) was heated on a wire screen in a conical flask of 50 ml volume, and to the aniline was added in small portions, with very vigorous hand shaking, over a period of 10-15 minutes, finely-ground, dry sulfaminic acid in the amount of 0.1 mole (9.7 g). Care was taken that the sulfaminic acid did not adhere to the bottom and to the walls of the flask. During the addition of sulfaminic acid, the temperature of the reaction mixture, as measured by a thermometer immersed in it, was maintained in the range 160-170°. After all of the sulfaminic acid had been added, the reaction mixture was boiled gently for 5 minutes. After cooling, the reaction mixture crystallized to a light pink, solid mass. To remove aniline, the mixture was washed 3 times with 30 ml portions of dry benzene, each time mixing the whole mass thoroughly. The viscous mass after a third washing became crumbly and hard. After 15 minutes the product was filtered off with suction and washed on the filter, mixing thoroughly each time, with 15 ml portions of benzene, and 3 times with 15ml portions of absolute ether. Following this the product was dried in

vacuo over sulfuric acid. The crude ammonium salt of phenylsulfaminic acid represented a fine crystalline, almost colorless, powder. Yield was 17.0 g (89.4% of the theoretical).

Reaction of Phenylsulfaminic Acid Ammonium Salt with p-Nitrobenzoic Acid. 0.01 mole of p-nitrobenzoic acid (1.67 g) and 5.0 ml of dry pyridine were heated to the dissolution of the acid, and to the solution was immediately added, with vigorous hand shaking, 0.01 mole crude ammonium salt of phenylsulfaminic acid (1.9 g). The salt at first dissolved immediately, and then rapidly precipitated considerable sediment, and the mixture became yellow. The reaction mixture was heated for 2 hours on a reflux, in an oil bath at 115°. During that time the sediment almost completely went into solution but the liquid remained turbid. The pyridine was distilled in vacuo, and to the residue was added 25.0 ml of 1.0 N caustic soda solution, the finely, crystalline, almost colorless precipitate filtered off with suction and washed 4 times with 5 ml portions of water. Yield of p-nitrobenzoic acid phenylamide was 0.75 g (30.9% of theoretical), m.p 206-208°; after recrystallization from 15 ml of butanol – large, flat needles, m.p. 210-211°; did not give depression with known p-nitrobenzanilide.

Interaction of Diphenylsulfamide with Two Molecules of p-Nitrobenzoic Acid. 0.01 mole of p-nitrobenzoic acid (1.67 g), 0.005 mole of diphenylsulfamide (1.24 g) and 5.0 ml of dry pyridine mixture were heated for 6 hours on an oil bath at 115°. The pyridine was distilled off in vacuo, and to the residue was added 25.0 ml of caustic soda solution. After 15 minutes the crystalline precipitate was filtered off with suction and washed 4 times with 5.0 ml portions of water. The crude p-nitrobenzanilide – fine gray crystals with m.p. 208-210° – did not give a depression with known nitrobenzanilide. Yield 1.78 g, i.e., 147.2% of theory, calculating on the basis of the general scheme of amidation, or 73.6% of theory, considering that the phenylsulfaminic acid is also an amidating agent. After recrystallization from 25.0 ml of butanol, large, flat needles resulted with m.p. 210-211°

Interaction of Sulfamide p-Nitrobenzoic Acid and Aniline. 0.01 mole of sulfamide (0.96 g), 0.02 mole of aniline (1.86 g), 0.01 mole of p-nitrobenzoic acid (1.67 g) and 5.0 ml of dry pyridine mixture were heated for 3 hours on an oil bath at 115°. The pyridine was distilled off in vacuo, and to the residue was added 25 ml of 2.0 N hydrochloric acid. The precipitated, finely crystalline, almost colorless crystals were washed 4 times with 5.0 ml portions of water, and then treated on the funnel with 10.0 ml of 1.0 N caustic soda solution, and again washed 4 times with 5 ml portions of water. From the alkaline filtrate upon acidification 0.12 g separated, i.e., 7.2% on the basis of p-nitrobenzoic acid used. M.p. 234-236° did not give a depression with known p-nitrobenzoic acid. 1.86 g of product insoluble in alkali, was obtained, i.e., 112% of theory on the basis of amide; on the basis of phenylamide – 76.9% of theory. The product melted slowly in the range 170-191°, and represented a mixture of amide and phenylamide. To separate, all of the mixture (1.86 g) was boiled with 100 ml of water, the undissolved portion (phenylamide) filtered off from the boiling solution with suction and washed twice with 5 ml portions of boiling water. 1.2 g of crude p-nitrobenzanilide with m.p. 199-205° resulted; melting point of the mixed sample with p-nitrobenzamide was 160-190°. After recrystallization from 25 ml of butanol large flat needles resulted, with m.p. 210-211°.

The aqueous filtrate from p-nitrobenzanilide was heated to boiling, cooled to 75°, and at the same time a small quantity of very fine crystals separated out, which were filtered off. After cooling, very nice long needles of p-nitrobenzamide separated out. Yield was 0.36 g, m.p. 195-197°; mixed sample with known p-nitrobenzamide melted at 19[illegible]-197°. Thus, the loss upon separation and crystallization constituted 0.3 g. Insofar as the unsubstituted amide is more readily soluble, this accounts for the loss of 0.2 g. and for the phenylamide 0.1 g. Accordingly, the total yield of phenylamide was about 1.3 g, i.e. about 50% of theory, calculating on the basis of p-nitrobenzoic acid entered into reaction, and the yield of unsubstituted amide about 0.53 g. about 36% theoretical, calculating also on the basis of p-nitrobenzoic acid, entered into reaction.

Phenylation of Sulfamide by Aniline in Pyridine Solution. 0.01 mole of sulfamide (0.96 g), 0.02 mole of aniline (1.86 g) and 5.0 ml of dry pyridine mixture were heated for 6 hours on an oil bath at 115°. The pyridine was then distilled off in vacuo, and to the residue was added 15.0 ml of 2.0 N hydrochloric acid, and the liquid extracted 3 times with 50 ml portions of ether. The ether extracts were washed three times with 3 ml portions of water and then extracted by 5 ml of 1.0 N caustic soda solution. 2.0 ml of 10.0 N sulfuric acid was added to the alkaline extract, at which time an oil separated which rapidly crystallized. The product was filtered off with suction, washed with water and dried in air. The yield of diphenylsulfamide was 0.35 g (14.1% of theory), m.p. 108-111°, and did not give depression with known sample of diphenylsulfamide. The aqueous mother liquor contained monophenylsulfamide. A better yield resulted when sulfamide was heated with a very large excess of aniline (10.0 ml of aniline for 0.01 mole of sulfamide) at 115°. According to A. Paquin [7], diphenylsulfamide results in 84% yield upon heating equimolecular quantities of aniline and sulfamide at 120-155° for 5.5 hours. This is inaccurate, since under such conditions only 10-15% of diphenylsulfanide results.

Interaction of p-Nitrobenzamide and Aniline in Pyridine Solution. 0.01 mole of p-nitrobenzamide (1.66 g), 0.02 mole of aniline (1.86 g) and 5.0 ml of dry pyridine mixture were heated for 3 hours on an oil bath at 115°. The

pyridine was distilled off in vacuo, the residue was treated with 25.0 ml of 2.0 N hydrochloric acid and after 10 minutes the undissolved crystalline precipitate was filtered off with suction and washed 4 times with 5 ml portions of water. 1.51 g of p-nitrobenzamide resulted, with m.p. 195-197°, which did not give depression with known p-nitrobenzamide.

Benzoylsulfaminic Acid Interaction with Aniline. 0.01 mole of betainopyridinium-sulfaminic acid (1.59 g) and 0.01 mole of benzamide (1.21. g) mixture was heated on an oil bath to melting at 160°, plus an additional minute [8]. To the resulting melt was then added 0.02 mole of aniline (1.86 g) and the mixture was heated on an oil bath at 120° for 2 hours. After cooling, 20 ml of water was added, , the fine crystalline precipitate was filtered off with suction and then washed twice with 5 ml portions of water, once with 5 ml of 1.0 N soda solution, 4 times (in 5 ml portions) with water and 3 times with 1 ml portions of alcohol. The yield of benzanilide was 0.35 g (70.4% of theory, based upon benzamide entered into reaction), m.p. 160-161°, and did not give depression with known benzanilide. After recrystallizing from 5 ml of alcohol, the benzanilide resulted in the form of large lustrous flakes, with m.p. 161-162°.

The aqueous filtrate from the benzanilide was acidified with hydrochloric acid to an acid reaction with Congo, and extracted 5 times (in 50 ml portions) with ether. The ether extracts were dried with Na_2SO_4, the ether distilled off to a volume of about 5 ml and the large transparent prisms which separated out were washed 3 times with 1 ml portions of ether. Yield of benzamide was 0.75 g, m.p. 126-127°, and did not give depression with known benzamide. From the ethereal mother liquor an additional 0.16 g of benzamide, with m.p. 122-126°, was isolated. Total yield of benzamide was 0.91 g (75% of the initial quantity).

SUMMARY

A theory for the amidation mechanism of carboxylic acids by sulfuric acid amides has been proposed and experimentally confirmed.

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• See Consultants Bureau translation, p. a-675.
•• See Consultants Bureau translation, p. 1713.
••• See Consultants Bureau translation, p. 1653.

THE ABNORMAL REDUCTION OF β-SUBSTITUTED PROPIONITRILES ACCORDING TO VYSHNEGRADSKY

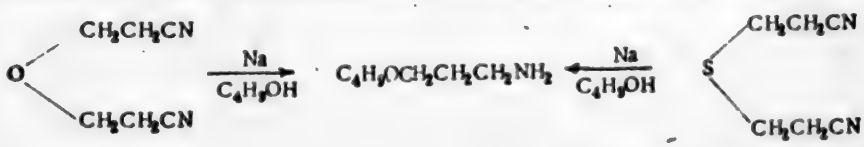
A. N. Kost and V. G. Yashunsky

The method of reducing organic compounds by the use of metallic sodium in an alcoholic medium was proposed for the first time in 1879 by a student and co-worker of A. N. Butlerov – a Russian scientist by the name of A. N. Vyshnegradsky [1]. While studying alkaloid structure, Vyshnegradsky obtained ethylpiperidine from ethylpyridine by this method. His untimely death in 1880 disrupted these brilliant experiments. In 1884, a German scientist, Ladenburg, applied the Vyshnegradsky method to the reduction of other pyridine homologs, and having somewhat modified the method of synthesizing bases, attributed this discovery to himself [2]. The Vyshnegradsky method was extended further to include various classes of organic compounds. It was found that not only could heterocyclic bases of the pyridine or quinoline type be reduced, but also nitriles, oximes, amides, ketones, lactones, esters, halogen derivatives, certain aromatic compounds, and others. At the present time the Vyshnegradsky method is widely used by chemists for the investigation of organic chemical structure, or for preparatory purposes. The qualitative determination of halogens according to Stepanov is based upon this method. A. N. Vyshnegradsky's priority is unquestionable; however, this method is frequently attributed to Ladenburg,, or even to Buvo, while the latter only applied the Vyshnegradsky method to the reduction of esters [3].

In the preceding articles [4,5] several examples of the application of Vyshnegradsky's method to the synthesis of certain diamines from aminonitriles was described. At the same time, the authors pointed out some instances of abnormal reactions, namely that small additions of potassium to sodium markedly lower amine yields, but when the potassium content reaches 2%, the yield again increases [6].

Reduction of nitriles, according to Vyshnegradsky, proceeds differently, depending upon the initial nitrile structure. It is known that upon reduction by sodium in alcohol, some nitriles become split at the CN groups with formation of the corresponding hydrocarbon + sodium cyanide. Thus Walter and McElvain [7], by reduction of benzonitrile, obtained benzylamine, but only in 7% yield, and from phenylacetonitrile they obtained toluene (in 90% yield). Likewise, during the reduction of diphenylacetonitrile, there was obtained, along with the corresponding amine, a considerable quantity of diphenylmethane [8]. During the reduction of α-aminoisobutyronitrile, isopropylamine was isolated [9], and the nitrile of α-phenylcinnamic acid converted almost completely into α,β-diphenylethane [10].

The authors have indicated earlier that an eight-membered piperazine analog results from dicyandiethylamine, namely, 1,5-diazacyclooctane [5]. It was of interest to reduce other dinitriles of the same type under the same conditions: $NCCH_2CH_2XCH_2CH_2CN$, where X = CH_2, O, S. During reduction of pimilonitrile (X = CH_2), the authors did not succeed in isolating the cyclic compound, and instead heptamethylenediamine resulted in 72% yield, which corresponded to the data of Brown [11]. During reduction of β,β'-dicyandiethylester (X=O) by sodium in butyl alcohol, the authors did not obtain a fraction corresponding to the linear diamine, but rather a considerable quantity of lower boiling substance resulted, which, from the constants and by analysis, was erroneously taken by the authors to be the cyclic amine, i.e., 1-oxy-5-azacyclooctane [12]. However, when the authors reduced β,β'-dicyandiethylsulfide (X = S) under the same conditions, it was then found unexpectedly that the reaction product was exactly identical with the one resulting from reduction of its oxide analog. By an investigation of the structure through its spectrum and by alternate synthesis, it was established in both cases α-butoxypropylamine resulted (with yields of 58.6 and 21.9% respectively).

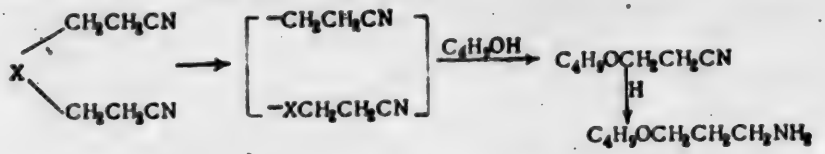


Seeger [13] observed a similar phenomenon when heating esters and nitriles of β-alkoxypropionic and butyric acids with alcohols in the presence of metallic sodium. He found that there occurs an exchange of the alkoxy

group for the radical of the alcohol introduced into the reaction. Thus from a 4-hour heating of 1 mole of β-methoxyisobutyronitrile, 5 moles of allyl alcohol and 5 g of metallic sodium mixture, β-allylhydroxyisobutyronitrile was isolated.

A comparatively easy cleavage of the dicyandiethyl ester was observed earlier during catalytic hydrogenation. Thus, Whitmore and his co-workers [14] found that upon hydrogenating this dinitrile over nickel catalyst, γ,γ-diaminodipropyl ester resulted; later, however, it was found that in reality a mixture of this diamine with propanolamine is formed [15].

The authors' experiments have shown that upon reduction with sodium in alcohol of the corresponding sulfide of the dicyandiethyl ester, cleavage occurs at the C-O or at the C-S bonds. The nitrile group is reduced only after addition of the alcohol. The linear amine, even upon thorough search, was not found by the authors.



For an explanation of the transformation mechanism which occurs, the authors have used simpler forms, namely the β-alkoxypropionitriles. It was found that if a propionitrile was used, with the same β-alkoxy group as for the alcohol in which the reaction was carried out, that a normal reaction product will result in the Vyshnegradsky reaction, i.e., the amine corresponding to the nitrile introduced, for example, β-ethoxypropionitrile in ethyl alcohol gives γ-ethoxypropylamine.

In the case where alkoxynitrile and alcohol radicals did not coincide, then in the final outcome, β-alkoxypropylamine with the alkoxy group of the alcohol was formed in the reduction.

Thus, upon reducing β-methoxypropionitrile and β-(β-hydroxyethoxy)-propionitrile in n-butyl alcohol, the authors isolated in both cases γ-butoxypropylamine. Upon reducing β-phenoxypropionitrile in ethyl alcohol, the authors obtained γ-ethoxypropylamine in 55% yield, while at the same time in almost all cases the normal reaction products were not found (Table 1).

TABLE 1

Reduction of β-Alkoxypropionitriles

Alcohol in which reduction was carried out.	initial alkoxynitrile $ROCH_2CH_2CN$ R =	resulting amine $ROCH_2CH_2NH_2$ R =	boiling point		picrate melting point	yield (%)
			(°C)	(mm)		
ethyl	C_2H_5	C_2H_5*	54–55	39	–	48.2
ethyl	C_6H_5	C_2H_5	59–60	48	–	55.5
isopropyl	iso-C_3H_7	iso-C_3H_7	74–75	68	–	21.5
n-butyl	n-C_4H_9	n-C_4H_9	80–81	24	96°	50.5
n-butyl	CH_3	n-C_4H_9	69–70	18	96°	25.8
n-butyl	$HOCH_2CH_2$	n-C_4H_9	57–58	8	95.5°	29.4
isoamyl	iso-C_5H_{11}	iso-C_5H_{11}**	82–83	20	104°	51.6

An even more simple example seems to be that of ethylenecyanhydrin (i.e., β-hydroxypropionitrile), while at the same time there are data in the literature only for its catalytic hydrogenation [16].

The authors reduced β-hydroxypropionitrile with sodium in a number of alcohols (Table 2) and found that in all cases the γ-alkoxypropylamines with the alkoxy groups of the alcohol used were formed:

$$HOCH_2CH_2CN \xrightarrow[ROH]{Na} ROCH_2CH_2CH_2NH_2.$$

*During reduction of β-ethoxypropionitrile in ethyl alcohol, apart from the corresponding amine, the authors isolated a base with b.p. 116-117° at 18 mm, to which can be attributed, on the basis of constants and of analysis, the diamine structure resulting from reduction of cyanethylated γ-ethoxypropylamine:

(see next page for continued footnotes)

In every case, the authors failed to isolate γ-propanolamine and other bases from the reaction products.

TABLE 2

β-Hydroxypropionitrile Reduction

alcohol in which reduction was carried out	resulting amine $ROCH_2CH_2CH_2NH_2$ R =	boiling point of amine (°C)	(mm)	yield (%)
ethyl	C_2H_5	58–59	45	21.0
isopropyl	iso-C_3H_7	78–79	96	20.0
n-butyl	n-C_4H_9	98.5–99.5	117	20.0
isobutyl	iso-C_4H_9 ***	85–86	20	24.4
isoamyl	iso-C_5H_{11}	66–67	12	36.4

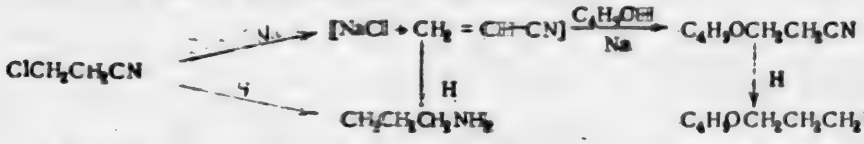
The explanation for the transformations during reduction by sodium in alcohols of β-alkoxypropionitriles can be given in two ways: either by direct realkylation of alkoxynitriles, or by intermediate formation of acrylonitrile, when this adds to the alcohol which has been used as the medium for the reaction, thus giving the corresponding alkoxynitrile. Subsequent reduction of the β-alkoxynitriles thus formed leads to the γ-alkoxyamines.

I. $ROCH_2CH_2CN + R'OH \xrightarrow{-ROH} R'OCH_2CH_2CN \xrightarrow{H}$
$R'OCH_2CH_2CH_2NH_2$;

II. $ROCH_2CH_2CN \rightarrow ROH + CH_2=CH-CN$;
$CH_2=CH-CN + R'OH \rightarrow R'OCH_2CH_2CN$;

$R'OCH_2CH_2CN \xrightarrow{H} R'OCH_2CH_2CH_2NH_2$.

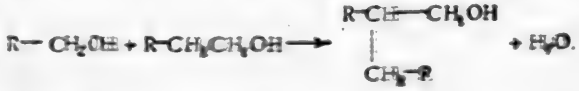
The second reaction course seemed more probable to the authors. This also confirms the reduction experiments of β-chlorpropionitrile in butyl alcohol. The authors isolated γ-butoxypropylamine in 68% yield, and some quantity of propylamine, i.e., the reaction course was as follows:



To verify these assumptions, the authors reduced acrylonitrile with sodium in a number of alcohols. As was to be expected, the principal reduction products were found to be γ-alkoxypropylamine, corresponding to the alcohols used.

From these experimental results it was found possible to make a deduction concerning the transformation mechanism which occurs in the abnormal Vyshnegradsky reaction, as discovered by the authors. Under the authors' conditions, β-hydroxypropionitrile is partially dehydrogenated, and the resulting acrylonitrile reacts further according to the scheme given. Low yields of alkoxypropylamines can be explained by the appearance of water in the reaction medium, and as is known, the reduction of nitriles or of esters by sodium in non-absolute alcohol gives poor yields of final products [17]. However, the authors failed to find at any time the presence of the acid which might be formed by hydrolysis of the nitrile.

Moreover, as has been shown by Guerbet [17a] and Terentyev [18], alcohols in the presence of alcoholates may enter into condensations of the type:



Under the authors' conditions this reaction could take place all the more readily, since the hydrogen atom of β-hydroxypropionitrile, by virtue of its being in the α-position to the nitrile group, is sufficiently mobile. The products of such condensation can undergo reduction and isolation of the resulting bases is quite difficult. Thus, with a certain degree of probability, the low yields of amines upon reduction of β hydroxypropionitrile can be explained. Reduction of β alkoxypropionitriles evidently proceeds according to scheme II given above. At the same time, a partial reduction of acrylonitrile to propylamine occurs. The resulting amine can be cyanethylated, while, on reduction, alkoxydiamines are produced.

$C_3H_7OCH_2CH_2CH_2NH_2 + CH_2=CH-CN \rightarrow [C_3H_7O(CH_2)_3NHCH_2CH_2CN] \xrightarrow{H} C_3H_7O(CH_2)_3NH_2$

In other experiments of similar type no fractions were isolated due apparently to their high boiling points.

•• γ-Isoamylpropylamine has been synthesized by the authors for the first time: n_D^{20} 1.4312; d_4^{20} 0.8517; MR_D 44.17; $C_8H_{19}ON$. Calculated MR_D 44.21

••• γ-Isobutoxypropylamine has been synthesized for the first time: n_D^{20} 1.4246; d_4^{20} 0.8448; MR_D 39.63; $C_7H_{17}ON$. Calculated MR_D 39.59. Picrate – m.p. 100°.

In the case of the dicyandiethyl ester, the cleavage products are found to be acrylonitrile and ethylene-cyanhydrin, while the latter may become partially dehydrogenated to acrylonitrile:

$$NCCH_2CH_2OCH_2CH_2CN \longrightarrow NCCH_2CH_2OH + CH_2{=}CH{-}CN;\ HOCH_2CH_2CN \longrightarrow CH_2{=}CH{-}CN + H_2O.$$

Reaction of the sulfide analog proceeds in a similar fashion.

Thus the authors have observed realkylation of β-halo, β-thio, β-hydroxy and β-alkoxy-propionitriles under the conditions of the Vyshnegradsky reaction. This phenomenon can be explained on the basis of mobility of the hydrogen atom which is in the α-position to the nitrile group, which facilitates ready splitting of the molecule, especially in alkaline medium. This reaction is reversible, but the acrylonitrile resulting from such a cleavage enters into reaction almost exclusively with the alcohol that has been used in the capacity of a medium for reduction, since this alcohol is present in large excess (nitrile: alcohol = 1:45). Thus the equilibrium is greatly shifted toward the right. Reduction of the nitrile group removes the nitrile from reaction, which shifts the equilibrium even more:

$$RX{-}\underset{\displaystyle H}{\underset{|}{CH}}{-}CH_2{-}CN \underset{\longleftarrow}{\overset{NaOR'}{\longrightarrow}} RX{-}H + CH_2{=}CH{-}CN;\ CH_2{=}CH{-}CN + R'OH \underset{\longleftarrow}{\overset{NaOR'}{\longrightarrow}} R'OCH_2CH_2CN;$$

$$R'OCH_2CH_2CN \xrightarrow{H} R'OCH_2CH_2CH_2NH_2.$$

If the β-alkoxy- or the β-thio-nitriles do not have α-hydrogens, then such nitriles should be transformed during the Vyshnegradsky reaction. In actuality, Cass [19] obtained a good yield of corresponding diamine during reduction of the nitrile from thiodipivalic acid.

It is interesting to note that during reduction of β-aminopropionitriles under the Vyshnegradsky conditions, there was not observed in noticeable quantities formation of any alkoxypropylamines. Apparently, the β-aminopropionitriles are stable in the presence of alkaline reagents.

EXPERIMENTAL

Synthesis of Pimelonitrile [20]. 38.2 g (0.165 mole) of 1,5-dibromopentane and 17.2 (0.35 mole) of a water-alcoholic solution of sodium cyanide were heated in a flask equipped with reflux condenser for 10 hours on a water bath. The alcohol was then distilled off, and the residue was redistilled with steam to remove unreacted dibromide. The remaining brown oil was extracted with ether, the ether solution washed with dilute alkali and dried over anhydrous calcium chloride, after which the ether was distilled off and the nitrile was fractionated at low pressure. 13.7 g (68% of theory) of the pimelonitrile resulted, b.p. 159-160° at 8 mm.

Literature data: b.p. 171-172° at 12 mm [20].

Synthesis of β-Alkoxypropionitriles. These were prepared by the authors according to the method of MacGregor [21], by the interaction of acrylonitrile with alcohols in the presence of sodium alcoholate.

β-Methoxypropionitrile. 0.9 g of metallic sodium was added to 24 g (0.4 mole) of methyl alcohol over a period of 30 minutes and with external cooling and stirring, there was added dropwise 21.2 g (0.4 mole) of freshly-distilled acrylonitrile. The mixture was then heated on a water bath with stirring for another hour, and was then neutralized with 20% sulfuric acid. The alcoholic layer was separated and dried with anhydrous sodium sulfate. 20.5 g (78% of theory) of β-methoxypropionitrile resulted with b.p. of 163-164°. β-Ethoxypropionitrile and β-isopropoxypropionitrile were obtained by the same procedure, with yields, respectively, of 76.8 and 71%. The nitrile constants corresponded with the literature data [22].

β-Isoamylhydroxypropionitrile. The alcoholate obtained by solution of 0.1 g of metallic sodium in 52.8 g (0.6 mole) of absolute isoamyl alcohol was placed in a three-necked flask equipped with mechanical stirrer, dropping funnel and reflux condenser. 31.8 g (0.6 mole) of acrylonitrile was added dropwise to the alcoholate (at 80° with stirring.). The mixture was then heated on a water bath, stirred for 1 hour and then neutralized with dilute sulfuric acid. The alcoholic layer was separated, dried with anhydrous sodium sulfate and redistilled. 64.2 g (75.9% theoretical) of β-isoamylhydroxypropionitrile resulted; b.p. 109-110° at 22 mm.

Literature data: b.p. 99° at 13 mm [23].

β-Butoxypropionitrile was obtained in the same manner with 78.5% yield.

β-Phenoxypropionitrile [24]. 121 g (1.28 moles) of phenol and 1.5 g of metallic sodium were placed in a three-necked flask equipped with mechanical stirrer, reflux condenser and dropping funnel. Then, over a period of one hour, and at 130-135°, 67.8 g (1.28 moles) of acrylonitrile was added, and the mixture stirred for another 5 hours at the same temperature. After cooling, the flask contents were treated with 10% caustic soda solution

and with ether. The ether layer was separated, washed repeatedly with the alkali solution, then with dilute hydrochloric acid and finally water. A crystalline mass remained after distilling off the ether. After recrystallization from cyclohexane —white flakes with m.p. 62°. 98.2 g of pure β-phenoxypropionitrile resulted (52% of theory).

Literature data: m.p. 61-62° [24].

β-(β'-Hydroxyethoxy)propionitrile. 39.8 g (0.75 mole) of acrylonitrile was added dropwise over a period of 2 hours to a cooled mixture of 46.5 g (0.75 mole) of ethylene glycol and 1.8 g of 25% aqueous caustic soda solution. The resulting yellow viscous mass was neutralized with dilute sulfuric acid. The organic layer was separated, dried with sodium sulfate, and fractionally distilled. Unreacted acrylonitrile was distilled off at atmospheric pressure, and the distillation then continued at decreased pressure. Three fractions were collected: I) up to 100° at 5 mm (mainly ethylene glycol); II) b.p. 132-135° at 5 mm —44.6 g; III) b.p. 160-171° at 3 mm —25 g.

The second fraction —monocyanethylated ethyleneglycol —was distilled repeatedly; b.p. 111-112° at 1.5 mm. Yield 47.8 g, calculated for acrylonitrile; n_D^{20} 1.4443; d_4^{20} 1.0793; MR_D 28.35; calculated 28.29.

The third fraction corresponded to dicyanethylated ethylene glycol, b.p. 186° at 9 mm [25]; 158° at 2 mm [26].

β,β'-Dicyandiethyl Ester. This ester was obtained by Bruson's method [27], by the interaction of acrylonitrile with ethylenecyanhydrin in the presence of alkali. B.p. 164-165° at 8 mm, which corresponded to the literature data [27].

β,β'-Dicyandiethylsulfide. The authors obtained this ester by reacting acrylonitrile with an aqueous solution of sodium sulfide [28]. 79.5 g (1.5 moles) of acrylonitrile was added to a solution of 180 g (0.75 mole) of the nona-hydrate of sodium sulfide in 100 ml of water, with stirring and cooling to 10°. After addition of the acrylonitrile, the mixture was stirred for 4 hours at room temperature, following which 200 ml of benzene was added. The benzene layer was separated, and the aqueous layer washed several times with benzene. The benzene solutions were combined, washed with small portions of dilute hydrochloric acid and water, and then dried over anhydrous sodium sulfate. The benzene was distilled off and the residue redistilled in vacuo. 89 g of β,β'-dicyandiethylsulfide resulted (i.e. 85% of theory). The viscous, colorless liquid crystallized upon standing. B.p. 178-179° at 3 mm.

Literature data: b.p. 191-194° at 7 mm [29].

β-Chloropropionitrile. Prepared through the action of dry hydrogen chloride upon acrylonitrile with cooling. B.p. 59-60° at 8 mm, which corresponded to the literature data [30].

Reduction of Pimelonitrile

A heated solution of 8.9 g (0.073 mole) of pimelonitrile in 330 ml of absolute n-butyl alcohol was added to 22 g of metallic sodium placed in a liter round-bottomed flask, equipped with a two-horned adapter and a heavy-duty copper reflux condenser. An oil bath preheated to 145° was immediately placed under the flask. This temperature was maintained until the sodium had completely dissolved; after that the mixture was cooled, and the resulting alcoholate decomposed with water. The alcohol and the base were distilled off over a period of several hours with superheated steam into a receiver containing dilute hydrochloric acid. From this solution the butyl alcohol was distilled out with steam, and the residue was condensed on a water bath. The crude hydrochloride was decomposed with powdered sodium hydroxide and the resulting base was repeatedly extracted with ether. The ether solution (about 300 ml) was dried with anhydrous caustic potash, and was fractionated after distilling off the ether. The first fraction —up to 91° at 7 mm negligible. The second fraction —heptamethylenediamine, with b.p. 91-92° at 7 mm —was collected in the amount of 6.41 g, which constituted 71.5% of theory. Upon standing, the diamine crystallized to form low-melting crystals. Benzoyl derivative —colorless needles from alcohol; m.p. 123°.

Literature data: b.p. 223-225°; benzoyl derivative —m.p. 123.5° [31].

Reduction of β,β'-Dicyandiethyl Ester

Reduction was carried out in like manner. 12.4 g (0.1 mole) of dicyandiethyl ester, 30 g of sodium and 430 ml of absolute n-butyl alcohol were taken. After reduction, the mixture was decomposed with water (100 ml).

The alcoholic layer was then separated, and the aqueous-alkaline residue washed with small portions of butyl alcohol. The combined alcoholic solution was acidified with hydrochloric acid and the alcohol distilled off with steam. The hydrochloride solution was concentrated on a water bath. The hydrochloride – a thick, light-brown oil – was decomposed with powdered caustic soda. The resulting base was repeatedly extracted with absolute ether. The ether solution was dried with anhydrous caustic potash and fractionated. The ether was distilled off first, and three fractions were then collected: I) b.p. up to 56° at 6 mm – 0.72 g; II) b.p. 56-60° at 6 mm – 7.63 g; III) b.p. 69.5-140° at 9 mm – 1.42 g.

During the second fractionation, 7.02 g (i.e. 53.6%) of γ-butoxypropylamine resulted, b.p. 74-76° at 20 mm, 169-170° at 756 mm; n_D^{20} 1.4288; d_4^{20} 0.8532; MR_D 39.61; calculated 39.59.

8.280 mg substance: 0.793 ml N_2 (23°, 740 mm) 8.670 mg substance: 0.831 ml N_2 (21°, 738 mm). Found %: N 10.75, 10.81. $C_7H_{17}NO$. Calculated %: N 10.68.

Literature data: b.p. 75-76° at 21 mm; n_D^{20} 1.4273; d_{20}^{20} 0.8514 [22].

Hydrochloride. Obtained by passing dry hydrogen chloride into an ester solution of the amine. Very hygroscopic.

Picrate. Obtained by heating the base with a saturated benzene solution of picric acid. Yellow rhombohedrons with m.p. 96°. Soluble in water, methyl and ethyl alcohols.

Benzoyl Derivative. Obtained by the Shotten-Baumann reaction. Viscous, slightly yellow liquid, b.p. 192-195° at 3 mm.

Chloroplatinate. Golden scales from aqueous alcohol; m.p. 199° (decomp.).

Reduction of β,β'-Dicyandiethylsulfide

1.72 g (21.9% of theory) of γ-butoxypropylamine with b.p. 69-70° at 16 mm was isolated after reduction of 8.3 g of β,β'-dicyandiethylsulfide, obtained by the action of 10 g of metallic sodium in 270 ml of absolute butyl alcohol in the usual manner. Picrate – m.p. 96°. Melting point of the sample mixed with picrate obtained from the preceding experiment did not give depression. The remaining reduction products were not investigated.

Reduction of β-Alkoxypropionitriles

Reduction of β-Ethoxypropionitrile in Ethyl Alcohol (Method A). A heated solution of 14.1 g (0.14 mole) of β-ethoxypropionitrile in 250 ml of absolute ethyl alcohol was poured rapidly into 20 g of metallic sodium placed in a liter round-bottomed flask with horned adapter and heavy-duty copper reflux condenser. An oil bath preheated to 130-135° was placed immediately under the flask. This temperature was maintained until the sodium had completely dissolved. After termination of reaction, about 100 ml of water was added to the mixture while still warm, and the amine and alcohol were distilled off with steam into a receiver containing dilute hydrochloric acid, and then the acid solution of the hydrochloride was concentrated on a water bath. The hydrochloride, in the form of a viscous oil, was decomposed with solid caustic soda and repeatedly extracted with absolute ether. The ether solution was dried with anhydrous caustic potash and distilled in vacuo. Two fractions were collected: I) b.p. 54-55° at 39 mm – 6.95 g; II) b.p. 116-117° at 18 mm – 1.45 g.

The first fraction represented γ-ethoxypropylamine; n_D^{20} 1.4242; d_4^{20} 0.8697; MR_D 30.28; calculated 30.35.

Literature data: b.p. 134-136° at 732 mm; n_D^{20} 1.4201; d_4^{20} 0.8613 [22].

The high-boiling fraction – β-(β'-ethoxy)-propyltrimethylenediamine; n_D^{20} 1.4512; d_4^{20} 0.9040; MR_D 47.75; calculated 47.81.

Its picrate was obtained upon heating the amine with a benzene solution of picric acid. After recrystallization from benzene, m.p. 143°.

7.495 mg substance: 1.190 ml N_2 (22°, 752 mm); 5.587 mg substance: 0.880 ml N_2 (22°, 752 mm). Found %: N 18.18, 18.03. $C_{24}H_{26}O_{15}N_8$. Calculated %: N 18.12.

β-Isopropoxypropionitrile Reduction (Method B). 14 g of metallic sodium was dispersed in hot toluene (50 ml) with a mechanical stirrer in a three-necked flask equipped with reflux condenser and dropping funnel. Then, over a period of 15 minutes, with stirring, 11.3 g (0.1 mole) of β-isopropoxypropionitrile in 60 ml of absolute isopropyl alcohol was added. For the solution of all sodium, 40 ml more of alcohol was added. Further treatment was carried out in a manner identical with the isolation of γ-ethoxypropylamine.

2.52 g (21.5% of theory) of γ-isopropoxypropylamine resulted after fractionation of the base. B.p. 74-75° at 68mm. According to the literature data: b.p. 85-86° at 102 mm [22].

γ-Butoxypropylamine. Obtained in yield of 50% from reduction of β-butoxypropionitrile in absolute butyl alcohol: b.p. 80-81° at 24 mm.

By the same method β-isoamylhydroxypropionitrile was reduced in absolute isoamyl alcohol. There resulted from 14.1 g of the nitrile, 7.5 g of γ-isoamylhydroxypropylamine, with b.p. 82-83° at 20 mm; n_D^{20} 1.4312; d_4^{19} 0.8517. MR_D 44.17; calculated 44.21.

Picrate—from benzene; m.p. 104°.

6.703 mg substance: 0.882 ml N_2 (23°, 754 mm). 7.802 mg substance 1.055 ml N_2 (24°, 755 mm). Found %: N 15.06, 15.11. $C_{13}H_{20}O_8N_4$. Calculated %: N 14.97.

Upon reducing 10.5 g (0.123 mole) of β-methoxypropionitrile in absolute butyl alcohol by method A, 4.15 g (25.8% of theory) of γ-butoxypropylamine with b.p. 69-70° at 18 mm resulted. Low boiling fraction —0.6 g of uncharacterized substances.

Upon carrying out by the same method the reduction of 11.5g (0.1 mole) of β-(β'-hydroxyethoxy)-propionitrile in butyl alcohol yielded 3.85 g (29.4%) of γ-butoxypropylamine with b.p. 57-58° at 8 mm; n_D^{18} 1.4280. d_4^{19} 0.8538.

Melting point of a sample of the picrate mixture from the γ-butoxypropylamine of the last two experiments with the picrate of γ-butoxypropylamine obtained by reduction of β-butoxypropionitrile in butyl alcohol did not give depression.

Reduction of β-phenoxypropionitrile was carried out according to method B, in ethyl alcohol without stirring of the reaction mixture. During the treatment which was identical with isolation of the alkoxy-propylamines, 5.72 g of γ-ethoxypropylamine with b.p. 59-60° at 48 mm (yield 55.5%) resulted, and 0.2 g of substance with b.p. 100-104° at 12 mm, the composition of which was not determined. The authors were not able to obtain any noticeable quantities of the base when they attempted to isolate γ-pheroxypropylamine by extraction of the aqueous-alkaline solution remaining after steam distillation.

β-Hydroxypropionitrile (Ethylenecyanhydrin) Reduction. A solution of 8.52 g (0.12 mole) of ethylene-cyanhydrin in 180 ml of absolute ethyl alcohol was heated to boiling in a round-bottomed flask equipped with reflux condenser and horned adapter. 16 g of metallic sodium was then dropped into the solution in 2-3 g lots. After dissolution of the metal, the alcoholate was decomposed with water and distilled with steam. The acidified distillate was evaporated and the hydrochloride decomposed in the usual manner. 2.6 g of γ-ethoxypropylamine resulted, with b.p. 58-59° at 45 mm. Hydrogenated acrylic acid was not found in the alkaline residue from distillation with steam. To separate the propanolamine, this solution was placed in a flask with a low outlet tube and was distilled to dryness. 30-40 ml of water was then added and redistilled to dryness. This operation was repeated twice. The distillate was placed in a Favorsky flask with tall dephlegmator, and water distilled out at 110°. The residue, about 1.5 g of viscous liquid, was not a base and did not have a defined boiling point.

By reduction of ethylenecyanhydrin (10.7 g, i.e. 0.15 mole) with sodium (19 g) in isopropyl alcohol (290 ml) by method B there resulted 3.26 g (20%) of γ-isopropoxypropylamine, b.p. 78-79° at 86 mm.

By reduction of ethylenecyanhydrin in isobutyl alcohol by method A, γ-isobutoxypropylamine resulted, in 24.4% yield. b.p. 65-66° at 20 mm. n_D^{18} 1.4246. d_4^{18} 0.8448. MR_D 39.63, calculated 39.59.

Picrate—m.p. 100° (from benzene).

8.595 mg substance. 1.184 ml N_2 (22°, 746 mm). 7.015 mg substance 0.980 ml N_2 (22°, 746 mm). Found %: N 15.64, 15.67. $C_{13}H_{18}O_8N_4$. Calculated %: N 15.55.

An attempt to separate propanolamine from the reaction products also gave negative results.

Upon reducing ethylenecyanhydrin in n-butyl alcohol by the same method, the authors obtained γ-butoxypropylamine in 20% yield.

The ethylenecyanhydrin was reduced in isoamyl alcohol by Method B. 4.26 g (0.06 mole) of ethylene-cyanhydrin and 13 g of sodium in 290 ml of absolute isoamyl alcohol were taken, i.e. one-and a-half times

more than in the preceding experiments. 3.17 g of γ-isoamylhydroxypropylamine (36.4% of theory) was separated; b.p. 66-67° at 12 mm.

Reduction of β-Chloropropionitrile. Reduction was carried out in n-butyl alcohol according to Method B. γ-Butoxypropylamine, b.p. 78-79° at 23 mm (68% of theory) and propyl amine in the form of the hydrochloride (8.4%) were separated during processing of the reduction products.

SUMMARY

1. It has been found that upon reducing β-halo-, β-hydroxy-, β-alkoxy- and β-thiopropionitriles according to the method of Vyshnegradsky (with sodium in alcoholic medium), an abnormal reaction takes place, which leads to formation of γ-alkoxypropylamines, while the alkoxy group becomes the radical of that alcohol in which medium the reduction is carried out.

2. The mechanism of this reaction has been investigated, and it has been proved that the process goes through a stage of acrylonitrile cleavage, with subsequent cyanethyiation of the alcohol and reduction of the alkoxynitrile thus formed.

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THE MECHANISM OF OXIDATION AND NITRATION OF CYCLOHEXANE BY NITRIC ACID AND NITROGEN OXIDES. I

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The oxidation and nitration of cyclohexane by nitric acid were investigated by Markovnikov [1], Nametkin [2] and Aschan [3]. From the point of view of classical organic chemistry, this reaction was most thoroughly studied by S. S. Nametkin.

The paraffin chain nitration theory developed by the author [4] made possible the determination of this reaction mechanism and discovery of new approaches. According to the author's theory, the initial stage of oxidation and nitration of cyclohexane, both by nitric acid and by nitrogen oxides, is the appearance of the free cyclohexyl radical during successful collisions of hydrocarbon with the radical monomer of nitrogen dioxide:

$$C_6H_{12} + NO_2 \longrightarrow C_6H_{11}\cdot + HNO_2. \quad (1)$$

Further, the principal transformation of cyclohexane in the nitration zone can be represented by Reactions 2-5:

$$C_6H_{11}\cdot + NO_2 \rightarrow C_6H_{11}NO_2 \quad (2)$$

$$C_6H_{11}\cdot + NO_2 \rightarrow C_6H_{11}ONO \quad (3)$$

$$C_6H_{11}\cdot + N{=}O \longrightarrow C_6H_{11}N{=}O, \quad (4)$$

$$C_6H_{11}\cdot + O{=}N(O)O{-}N{=}O \longrightarrow C_6H_{11}ONO + NO_2. \quad (5)$$

During nitration in the liquid phase at elevated temperatures, the significance of directions (4) and (5) will be small, with a few exceptional cases, and consequently the principal primary reaction products will be nitrocyclohexane and cyclohexylnitrite. Nitrocyclohexane should survive as a final reaction product, and cyclohexylnitrite, through intermediate formation of cyclohexanol, should be transformed into a mixture of adipic and lower dicarboxylic acids.

According to the author's theory, nitric acid should not exert independent oxidizing and nitrating actions. It affects the rate and the ratio between the principal direction of the reaction only through its participation in the equilibrium $2HNO_3 + NO \rightleftarrows 3NO_2 + H_2O$, which serves as the source and the means for progressive regeneration of nitrogen dioxide from the lower oxides. At high temperatures, the pyrolysis products of nitric acid: nitric anhydride, nitrogen trioxide, NO_3, NO_2, and so forth, may prove to be active. Experiments confirmed these deductions from the general nitration theory of the paraffinic chain. It was first of all demonstrated that cyclohexane reacts noticeably with nitrogen dioxide at normal temperature, and comparatively rapidly at 100°. Under appropriate conditions, the reaction leads to the formation of adipic acid and nitrocyclohexane for the most part, i.e., the same products as from the interaction of cyclohexane with nitric acid.

Furthermore, by carrying out the reaction with nitric acid under the same conditions as with nitrogen dioxide, and also according to the S. S. Nametkin method, the authors have proved that interaction almost ceases in the absence of nitrogen dioxide in the reaction zone, and the rate of its reaction was found to be proportional to the addition of NO_2. Moreover, during oxidation by nitrogen dioxide, the addition of nitric acid in the corresponding cases affected reaction yields negatively, due to the presence of water in the acid used and due to a shift to the right of the equilibrium $3NO_2 + H_2O \rightleftarrows 2HNO_3 + NO$.

The reaction course in the gaseous phase, through interaction of cyclohexane with nitrogen dioxide, has been established by its accomplishment in sealed tubes at 100° by heating of the hydrocarbon and nitrogen dioxide mixture taken in such quantities as to ensure their complete vaporization. The absence of the oxidizing and nitrating action of nitric acid under these conditions results from nitration according to Nametkin, by the addition of ammonium sulfate, since the reaction is capable of occurring in the gaseous phase because the tubes were not more than one-third full.

Experimental proof of the absence of reaction between nitric acid and hydrocarbons at high temperature ($< 200°$) is extremely difficult to obtain due to the simultaneous self-decomposition of the nitric acid to form nitrogen dioxide. Moreover, it cannot be denied that at sufficiently high temperature the direct interaction of nitric acid with the paraffin chain may become noticeable; even more probable are reactions with pyrolysis products HNO_3–N_2O_5, NO_3·, NO_2, etc. And also, all of the experiments carried out at 320-340° demonstrated that the yields of reaction product upon interaction of cyclohexane with nitrogen dioxide were almost ten-fold greater than with analogous experiments using nitric acid of sp. gr. 1.4. With an increase in the duration of nitric acid remaining in the reaction tube, the yield of reaction product increased somewhat, which is explained by the increased possibility of its decomposition. These results at least indicate a low reaction rate with nitric acid, even at temperatures this high.

The radical character of the primary reaction between cyclohexane and nitrogen dioxide [1] is confirmed by various experimental data. This indicates possibility of its existence in the gaseous phase. There is practically no change in the reaction yield with increase in the quantity of nitric acid, and the large increase in reaction yield with an increase in the quantity of cyclohexane demonstrates its role in the hydrocarbon phase, which is also in agreement with the accepted radical character of the reaction. The absence of any noticeable acceleration of reaction between nitrogen dioxide and cyclohexane upon adding strong protonic and aprotonic acids – sulfuric acid, aluminum chloride, titanium tetrachloride and also iodine – indicates the insignificant role of the ionic character of interaction in the primary oxidation and nitration stage of the paraffinic chain.

The above-indicated traits are characteristic for nitration of cyclohexane, and are entirely different for the parent substance of aromatic compounds – benzene, with which there is a genetic relation. This corresponds to the general distinctions which are made between the nitration of saturated and of aromatic hydrocarbons, and the mechanisms accepted for them [5]. In agreement with the position indicated, the authors also found that the addition of mercury salts had little noticeable effect upon the nitration of cyclohexane.

In accordance with the adopted mechanism, the nitration and oxidation reaction of cyclohexane does not possess a chain character. This deduction was confirmed by the observation that there was no difference in reaction rates upon passing cyclohexane and nitrogen dioxide mixture through an empty tube in one experiment as against passing through a tube filled with glass chips in another. Apparently, however, at high concentration of nitrogen dioxide dimer, the development of sufficiently long chains is possible by such a scheme:

$$R{-}H + NO_2^{\cdot} \longrightarrow R^{\cdot} + HNO_2,$$

$$R^{\cdot} + N_2O_4 \longrightarrow RONO + NO_2^{\cdot},$$

$$NO_2^{\cdot} + R{-}H \longrightarrow R^{\cdot} + HNO_2, \text{ etc.}$$

The breaking of chains will occur at the expense of combination of radicals with NO and NO_2, branching at the expense of the side reactions of cyclohexylnitrite and cyclohexanol oxidation. It is very probable that such a case was realized experimentally by the authors when, upon heating 0.84 g of cyclohexane and 4.5 g of nitrogen dioxide in a sealed tube at 100°, the tube exploded with considerable shattering effect.

EXPERIMENTAL

The procedure for treatment of the nitration and oxidation product of cyclohexane was carried out according to the following method, with the following, or other, minor modifications. The reaction mass, which normally contained solid adipic acid, was filtered off with suction; the precipitate was washed with small quantities of cyclohexane and water, and after being dried in air, represented quite pure adipic acid with m.p. about 151°. The aqueous portion of the filtrate was evaporated to dryness on a water bath. The mixture of adipic, glutaric, succinic and oxalic acids which resulted from such procedure normally melted at 130-140°, but still consisted for the most part of adipic acid since it gave an increased melting point upon heating with the pure product. All of the cyclohexane was distilled off from the organic layer of the filtrate after washing with soda solution. The remaining crude nitro product, the greater portion of which redistilled at 20 mm pressure with a b.p. of 95-100°, had n_D^{20} 1.463 and possessed other properties approximating those for pure nitrocyclohexane. The authors observed that its dissolution in alkali was speeded up by additions of diethylamine, although not to such striking extent as was found earlier for phenylnitromethane.

Comparison of the Behavior of Cyclohexane With Nitrogen Dioxide and Nitric Acid.

a) Experiments at Normal Temperature in Sealed Tubes. A mixture composed of 10 ml of cyclohexane and 10 ml of nitric acid, sp. gr. 1.4, not containing any nitrogen oxides, in the first experiment, and a mixture composed of the same quantity of hydrocarbon with 6 g of nitrogen dioxide in the second experiment, were left

standing for 60 days in sealed tubes at 20-25°. No excess pressure was found upon opening the tube containing the nitric acid. Only traces of nitro products were isolated, formed possibly at the expense of nitrogen oxides that developed at random. A very high pressure was found in the second tube, and from the reaction product 0.20 g of nitrocyclohexane and 2.37 g of adipic acid —65% of the theoretical yield, resulted.

b) Experiments at 60° in an Open Container. The reaction with nitrogen dioxide was carried out in a three-necked flask. A mixture of 20 g of nitrogen dioxide and 50 ml of hydrocarbon was added to 350 ml of cyclohexane over a period of 16 hours, and with simultaneous passing through of 3 liters of oxygen. 5.1 g of adipic acid and 6.7 g of crude nitrocyclohexane were isolated from the reaction mixture.

Upon treatment of the nitroproduct with 10% KOH solution and with addition of diethylamine, with subsequent recrystallization of the undissolved residue from alcohol, there resulted a small quantity of colorless, crystalline substance with m.p. 216°. As melting of a mixed sample indicated, the substance isolated was apparently 1,1'-dinitrodicyclohexyl, obtained earlier by S. S. Nametkin, according to his method, during the nitration of cyclohexane.

The experiment carried out under the same conditions, but with application of 40 ml of nitric acid, sp. gr. 1.4, and with addition of 2 g ammonium nitrate instead of nitrogen dioxide, gave only traces of reaction products.

TABLE 1

Expt. No.	Additions	Obtained (g)	
		$C_4H_8(COOH)_2$	$C_6H_{11}NO_2$
1	—	1.2	0.8
2	1 g $(NH_4)_2SO_4$	—	Traces
3	1 g N_2O_4	1.8	1.6

TABLE 2

Expt. No.	Taken into reaction		Obtained (g)		Total yield (a + b) (in mole · 100)
	HNO_3 (ml)	N_2O_4 (g)	$C_4H_8(COOH)_2$ (a)	$C_6H_{11}NO_2$ (b)	
1	10	0.9	0.59	0.08	0.465
2	10	2.8	1.33	0.15	1.027
3	—	2.8	1.05	0.41	1.038

TABLE 3

Expt. No.	C_6H_{12} (in g)	Yield (in g)		Total yield (in mole · 100)	HNO_3 consumption (in %)
		$C_4H_8(COOH)_2$	$C_6H_{11}NO_2$		
1	0.21	0.03	Traces	0.020	0.68
2	0.42	0.10	Traces	0.068	2.23
3	0.84	0.25	Traces	0.169	5.80
4	1.68	0.59	0.08	0.466	14.20
5	3.36	1.76	0.98	1.940	48.50
6	5.23	1.92	1.73	2.520	58.0
7	9.24	2.36	2.05	3.170	70.30

c) Experiments in Sealed Tubes at 100°. 10 ml of cyclohexane was mixed in one case with 2 ml of nitrogen dioxide, and in the other —with 10 ml of nitric acid, spec. grav. 1.3, and with addition of 1 g ammonium sulfate, added to remove nitrogen oxides that might appear. The two mixtures were heated in sealed tubes at 100° for 3 hours.

1.08 g adipic acid and 2.00 g of crude nitrocyclohexane containing, as further investigation showed, a noticeable quantity of cyclohexylnitrite, were isolated from the cyclohexane + nitrogen dioxide reaction mixture. In the nitration experiment, almost no interaction of nitric acid occurred.

d) Experiments at Normal Pressure and at 320-330° in the Gaseous Phase (See [6]). Oxidation and nitration of cyclohexane by nitric acid was carried out with and without the presence of nitrogen dioxide. The first experimental series was carried out according to the method of S. S. Nametkin. One experiment was carried out in exact accordance with the literature directions, the second —with addition of ammonium sulfate to remove traces of nitrogen oxides contained in the normal nitric acid and which might appear during the reaction, and finally, the third —with preliminary addition of nitrogen dioxide. The basic charge for each of the tubes consisted of 10 ml of cyclohexane and 15 ml of nitric acid, sp.gr. 1.2. Heating of the sealed tubes was carried out in a horizontal oven at 103-107° for a period of 9 hours, during which, at two hour intervals, the excess pressure was let out. Data are given in Table 1.

In the second experiment – without nitrogen oxides – excess pressure was not found; the appearance of traces of nitroproducts can be explained by the impossibility of inhibiting the formation of small amounts of nitrogen oxides in the cyclohexane layer.

The effect of nitrogen dioxide quantity upon the reaction yield can be seen from the following series of experiments. The charge placed in each of the tubes consisted of 1.68 g of cyclohexane, varying quantities of nitric acid, sp.gr. 1.3, and nitrogen dioxide. Heating time in the horizontal water bath was 3 hours (Table 2).

The yield increased proportionately to the quantity of added nitrogen dioxide. In the third experiment (without addition of nitric acid) it was somewhat higher than in the similar experiment with addition.

Reaction in the Gaseous Phase at 100°. 0.5 g cyclohexane and 1.4 g of nitrogen dioxide were placed in a tube of 120 ml volume, so calculated that at 100° the substances taken for reaction would be completely converted to the gaseous state. After sealing and heating at 100° for 3 hours, there resulted 0.21 g of adipic acid and 0.04 g of nitroproduct.

Concerning the reaction course at 320-340°, see [6].

Effect of Quantity of Cyclohexane upon the Reaction Yield. The charge for each tube consisted of 10 ml of nitric acid, sp.gr. 1.3 (47.5%), 0.9 g of nitrogen dioxide and variable quantities of cyclohexane. Heating of the sealed tubes was carried out in a horizontal water bath for 3 hours (Table 3).

The extent of nitric acid consumption was calculated according to the stoichiometric equations:

$$3C_6H_{12} + 10HNO_3 = 3C_4H_8(COOH)_2 + 8H_2O + 10NO$$

and

$$C_6H_{12} + HNO_3 = C_6H_{11}NO + H_2O.$$

Taking into account the formation of lower dicarboxylic acids and CO_2, it should be considered that the true consumption of nitric acid was somewhat higher. The calculations indicate that in the first two cases reactions proceeded exclusively in the gas phase.

Investigation of the Action of Protonic and of Non-Protonic Acids. Addition of titanium tetrachloride, aluminum chloride and sulfuric acid to cyclohexane and nitrogen dioxide mixture caused no observable change. Nor was there found any accelerating effect by sulfuric acid additions to the cyclohexane-nitric acid mixture.

To test the actions of similar types of addition in relation to time, experiments were arranged with a mixture of 25 ml of cyclohexane and 6 g of nitrogen dioxide, to one portion of which was added 5 g of aluminum chloride, and to the other 2 g of iodine. Judging from the color intensity of nitrogen dioxide in the gaseous phase for the control experiment and in the test experiment upon adding aluminum chloride, the reaction rates in both experiments were very similar. Treatment of the reaction mixtures of the control and of the experimental tests after one month standing at normal temperature gave in all cases almost identical yields of reaction products – about 0.7 g of nitroproduct and the same quantity of adipic acid.

A rapid nitration course was observed by the authors during reaction of nitric anhydride with cyclohexane. The cyclohexane reaction, carried out with nitric acid in the presence of nitrogen dioxide in sealed tubes at 100° with additions of mercury nitrate indicated no effect for the latter.

SUMMARY

1. The interaction of cyclohexane with nitrogen dioxide proceeds with relative rapidity and gives the same products as nitration with nitric acid according to the method of Konovalov-Nametkin.

2. Oxidation and nitration of cyclohexane by nitric acid proceeds by way of an intermediate reaction with nitrogen dioxide.

3. The radical character of the primary reaction stage has been confirmed by its course in the gaseous and hydrocarbon phases, and by the absence of any accelerating action of strong protonic, aprotonic acids, or mercury salt additions upon it.

4. The nitration theory for the paraffinic chain, as earlier developed, is applicable to the oxidation and nitration of cyclohexane.

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THE REACTIONS OF ALIPHATIC DIAZO COMPOUNDS WITH UNSATURATED COMPOUNDS

XIV. REACTION OF DIAZOACETATE WITH HALOGEN DERIVATIVES OF THE ALIPHATIC-AROMATIC SERIES.

I. A. Dyakonov and N. B. Vinogradova

As was demonstrated earlier [1-3], halogen derivatives of hydrocarbons of the allyl type react with diazoacetate in the presence of copper catalyst according to the equation (1):

$$RX + N_2CHCOOC_2H_5 \xrightarrow[(CuSO_4)]{Cu} RCHXCOOC_2H_5 + N_2, \qquad (1)$$

where, for the examples investigated, R = Radical of $CH_2=CH-CH_2-$, and X = Cl, Br or I.* Since it was found that halogen derivatives of the non-allyl type (ter- and n-butyl bromides) do not readily enter into reaction [3], an attempt has been made to expand this reaction to include halogen derivatives of hydrocarbons of the aliphatic-aromatic series which possess a more mobile halogen atom: benzyl bromide, di- and tri-phenylbromomethanes.

The results of these experiments are described in the present article.

Investigation has shown that the reaction course for experiments with triphenylbromoethanes in the presence of copper sulfate as catalyst, and ligroin as diluent, may be expressed by equations (2) and (3):

$$(C_6H_5)_3CBr \xrightarrow[CuSO_4]{N_2CHCOOC_2H_5} \underset{(I)}{(C_6H_5)_2CCHBrCOOC_2H_5} + N_2; \qquad (2)$$

$$(I) \xrightarrow[61\%]{N_2CHCOOC_2H_5} BrCH_2COOC_2H_5 + (C_6H_5)_2C=\underset{\displaystyle C_6H_5}{\overset{\displaystyle |}{C}}COOC_2H_5 + N_2 \qquad (3)$$

(II)

$$(II) \xrightarrow[88\%]{NaOH} \underset{(III)}{(C_6H_5)_2C=\underset{\displaystyle C_6H_5}{\overset{\displaystyle |}{C}}COOH} \qquad (4)$$

The final reaction product expected in this case—the ethyl ester of β,β-diphenyl-α-bromohydrocinnamic acid (I)—was not separated from the reaction mixture: in the course of the synthesis, under the action of non-reacted diazoacetate, it immediately converted into the ester of triphenylacrylate (II) by splitting off HBr with rearrangement of the phenyl. •• The evolving hydrogen bromide became bound with the diazoacetate to form bromoacetate.

With a 1:1 molar ratio for the reactants, in ligroin, the yield of analytically-pure ester (II) was 60.9%, and the yield of bromacetate was 60.8% of the theoretical, calculating on the basis of original diazoacetate, and taking into account the combined equation resulting from equations (2) and (3).

The ester (II) was converted into triphenylacrylic acid (III) in 88% yield by the action of alkali. The yields of ester (II) cited in the literature are small [7] in connection with which it should be noted that the reaction described here may have a preparative value for its synthesis [and likewise for synthesis of acid (III)].

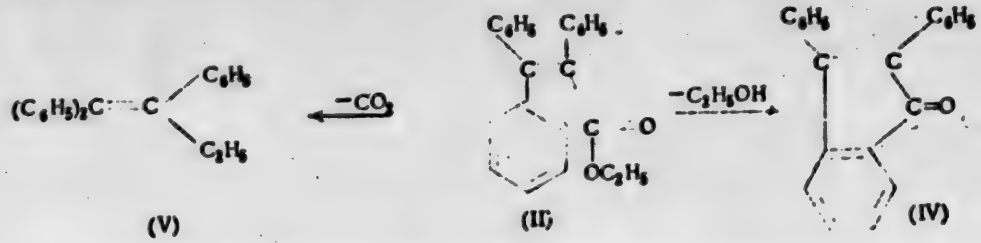
As the result of the same reaction course (2) in the absence of solvent, and at a temperature of 160-165°, there were obtained: the bromacetate, 1,1,2-triphenylbutene-1 (V) and diphenylindone (IV) (yields respectively 81.2, 78.0 and 4-5%). ••

• The reaction, upon which is based the diazo method for synthesis of simple organic compounds, is analogous to that quoted above (1) [4]. In Group IV, e.g. the halogenides of Si, Sn and Pb react in the indicated manner. In 1951 the authors [1], and a little later some American chemists [5], demonstrated that this reaction can also be extended to include certain halogen derivatives of hydrocarbons of the aliphatic series.

•• Rearrangement upon splitting off HX from halogen derivatives of the general formula $R-\underset{R_2}{\overset{R_1}{C}}-\underset{R_3}{\overset{H}{C}}-X$ have been adequately studied [6].

••• According to calculation for 0.5 mole of initial diazocetate.

The formation of compounds (IV) and (V) may be explained in the following manner. Under the conditions of the experiment, at a temperature of 160-165°, ester (II), which at first is formed primarily according to Equations (2) and (3), decomposes in two ways:

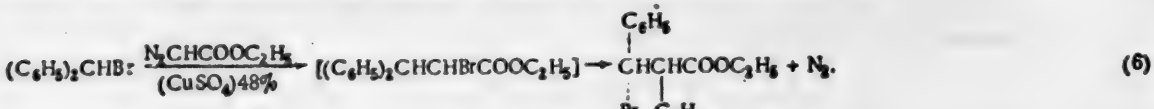


(V) (II) (IV) (5)

It is known from the literature data that diphenylindone actually forms as a side product in the synthesis of ester (II) at the expense of its partial intramolecular condensation [8].

Unknown up to the present time, hydrocarbon (V) is apparently formed also upon decomposition of the ester (II), because it was possible to find (qualitatively) CO_2 in the nitrogen evolving during the condensation reaction. This secondary reaction was not investigated in any more detail.

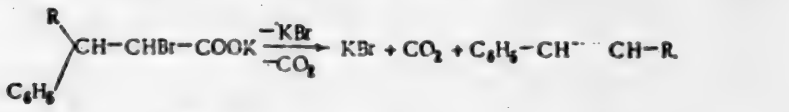
Condensation of diphenylbromethane with diazoacetate was carried out with a 1:1 molar ratio of reactant in the presence of cupric sulfate and in the absence of solvent, at a temperature of 80°. The reaction product corresponded in composition to the β-phenyl-α-bromhydrocinnamic acid ester (VI); however, further investigation has shown that it has the structure of the isomeric α-phenyl-β-bromhydrocinnamate (VII):

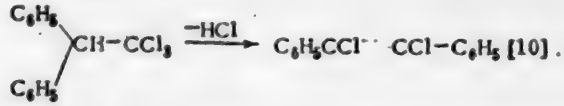


(VI) (VII) (6)

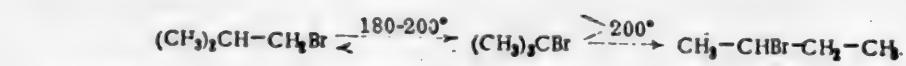
The authors are inclined to think that during the course of the reaction there occurs isomerization of the unstable normal reaction product (VI) into the more stable isomer (VII) with a symmetrical distribution of the phenyl groups.

The possibility of a similar isomerization of ester (VI) indicates the following known facts for other compounds. Rearrangements, with a change in the carbon framework, takes place when hydrogen halide acids split out from the esters which have a structure similar to (VI), or halogen derivatives of hydrocarbons with unsymmetrical distribution of phenyl groups (where R = C_6H_5, C_2H_5 [9]):





Halogen derivatives of the hydrocarbons of the aliphatic series isomerize with migration of the halogen atom within the carbon chain (A. E. Favorsky [11]) and sometimes irreversibly with a change in the carbon framework [12]:



It is quite possible that isomerization in the halogen derivative series of aliphatic-aromatic hydrocarbons will occur at lower temperature than in the aliphatic series (in our case – at 80°).

Ester (VII) is described here for the first time. Yield = 31.2% of theoretical for crude product with m.p. 110° (possibly a mixture of 4 diazostereoisomers) and 20.1% for the product with a constant m.p. of 132°. Since the bromacetic acid ester was also isolated from the reaction, and, after alkaline treatment, a small quantity of the acid corresponding to ester (VII), then it should be assumed that in this case a secondary reaction has been

substituted for that of the diazoacetate with the bromoester (VI) or (VII):

$$(VII)\ \text{or}\ (VI)\ \xrightarrow[17.2\%]{N_2CHCOOC_2H_5}\ BrCH_2COOC_2H_5 + C_2H_5-\underset{H}{\overset{}{C}}-\underset{C_6H_5}{\overset{}{C}}-COOC_2H_5. \qquad (7)$$

(VIII)

For determination of the structure of ester (VII), which at first was taken to be ester (VI), it was treated with alcoholic caustic alkali. Here, instead of the β-phenylcinnamic acid (IX), there was obtained the trans-α-phenylcinnamic acid (X).

With view in mind of the possibility of rearrangement upon the HBr cleavage reaction, the authors attempted to replace bromine by hydroxyl in the ester investigated, by reaction with aqueous rather than alcoholic alkali. However, instead of the β,β-diphenyllactic acid (XI) which was expected here, acid (X) again resulted. For proof of the structure, the latter was first oxidized with potassium permanganate, at which time benzoic and benzoylformic acids resulted, and were identified by mixed sample test with known acid (from benzaldehyde and sodium phenylacetate [13]).

$$(C_6H_5)_2C{=}CHCOOH \xleftarrow[(C_2H_5OH)]{KOH}\ (VI)\ \xrightarrow[(H_2O)]{KOH}\ (C_6H_5)_2CHCHOHCOOH. \qquad (8)$$

(IX) (XI)

$$(VII)\ \xrightarrow[(C_2H_5OH,\ H_2O)]{KOH}\ C_6H_5CH{=}C(C_6H_5)CO_2H\ (X)$$

$$C_6H_5CHO + C_6H_5CH_2COONa \xrightarrow[57\%]{KMnO_4}\ C_6H_5CO_2H + C_6H_5COCO_2H. \qquad (9)$$

The obtaining of acid (X) cannot be considered faultless proof of the bromester structure. For determination of the structure, it is necessary to select a reaction which will not affect the rearrangement centers i.e., the C-Br and C-H bonds in the molecule of this compound. The dealkylation reaction of the ester by the use of a strong HBr solution in glacial acetic acid was found to be suitable for this purpose. The α-phenyl-β-bromhydrocinnamic acid (XII) isolated as the result of the dealkylation, had a m.p. of 185° [13], in contrast to its isomeric form, β-phenyl-α-bromhydrocinnamic acid (with m.p. 164° [9]) and displayed all of the reactions characteristic for it. A sample of known acid (XII) was obtained (according to Müller [13]), for comparison, by reacting concentrated HBr with α-phenyl-cinnamic acid (X), and finally by esterification of the acid (XII) there was obtained the corresponding ethyl ester which was found to be identical with the ester (VII):

$$C_6H_5CHBrCHCOOC_2H_5 \xrightarrow[69\%]{HBr}\ C_6H_5CHBrCHCO_2H + C_2H_5Br. \qquad (10)$$

(VII) (XII)

$$C_6H_5CH{=}CCO_2H \xrightarrow[(CH_3COOH)]{HBr}\ C_6H_5CHBrCHCO_2H \xrightarrow[(93\%)]{C_2H_5OH}\ (VII). \qquad (11)$$

(X) (XII)

The yield of acid (XII) (crude product) by dealkylation, and of the ester (VII) from the esterification reaction, constituted, respectively, 69 and 93% of the theoretical yields. The reactions expressed by Equations (10) and (11) finally determined the structure of the ester (VII).

Benzyl bromide apparently reacts only to a small extent with the diazoacetate in the direction expected:

$$C_6H_5CH_2Br \xrightarrow[(Cu)]{N_2CHCOOC_2H_5}\ C_6H_5CH_2CHBrCOOC_2H_5 + N_2. \qquad (12)$$

(XIII)

The reaction is accompanied by formation of a considerable quantity of fumarate due to decomposition of unconsumed diazoacetate, and also by large amounts of tars.

A number of attempts to isolate the ester (XIII) from the resinous reaction product, or to prove its presence in it by the use of various reactions, was to no avail. Only dehalogenating reduction with Zn dust in acetic acid led to the isolation of a small quantity of ethyl hydrocinnamate (XIV), which was identified with the known by the hydrazide of the acid:

$$(XIII)\ \xrightarrow{Zn + CH_3COOH} C_6H_5CH_2CH_2COOC_2H_5\ \xrightarrow{NH_2NH_2}\ C_6H_5CH_2CH_2CONHNH_2. \qquad (13)$$

(XIV) (XV)

This result allows us to assert that Reaction (1) can be considered proved in principle.

It should be considered that an equation of the general form (1) [R = $C_6H_5CH_2$; $(C_6H_5)_2CH$; $(C_6H_5)_3C$; X = Br] encompasses all three types of interaction studied, outside of the question of whether additional reaction (1) is accompanied by isomerization, rearrangement, or HBr cleavage from its final product. The yield of Reaction (1) in a series of investigated halogen derivatives increased with an increase in the radical R.

EXPERIMENTAL

I. Condensation with Triphenylbrommethane in Ligroin. For a description of the apparatus (see [1 3]). 32.2 g of triphenylbrommethane [14] 100 ml of purified ligroin (b.p. 100-110°) and 0.2 g of anhydrous $CuSO_4$ were heated until the greater portion of triphenylbrommethane went into solution. After that 11.4 g of diazoacetate was added dropwise to the boiling solution with mechanical stirring.* 3.2 liters of nitrogen were evolved (15°, 758.8 mm).

The reaction mixture was filtered from the catalyst while hot. Upon cooling, the filtrate crystallized. The crystals were removed by suction and the ligroin mother liquor was further fractionated.

Ethyl Triphenylacrylate (II). After recrystallization from alcohol, 10 g (60.9% of the theoretical yield, calculated on the basis of diazoacetate) of crystals of almost colorless ester (II) resulted, with a m.p. of 119-120°. The ester gave with concentrated H_2SO_4 a characteristic green color, changing to ruby-red upon heating. The melting point and other properties corresponded to that indicated in the literature [15].

Found %: C 83.97; H 6.03; M 324.4, 317.1. $C_{23}H_{22}O_2$. Calculated %: C 84.10; H 6.14. M 328.4.

Bromacetate. Upon fractionating the ligroin mother liquor, a fraction of the substance with lachrymatory properties and with a boiling point corresponding to the bromacetate was obtained. Yield 18.2 g (60.8% of theoretical).

B.p. 156-161°; d_4^{18} 1.492; n_D^{18} 1.452.

Found %: Br 46.38. $C_4H_7O_2Br$. Calculated %: Br 47.90.

Literature data [16]: b.p. 159°; d_4^{18} 1.514; n_D^{18} 1.454.

Certain deviations in the analytical data between found and calculated should be attributed to the possible impurity of fumarate (See [2]).

Triphenylacrylic Acid (III). 1 g of the ester (II) was heated for 8 hours with 16.5 g of caustic potash dissolved in 70 ml of alcohol. The solution was diluted with water, the alcohol distilled off, and the residue in the distilling flask was diluted with water to 100 ml because of the difficult solubility of the potassium triphenylacrylate. The free acid (III) was separated from the solution by dilute sulfuric acid, in the cold. Yield – 0.8 g (87.9% of theoretical). B.p. 212-213°– which corresponds to the literature [8].

Found %: C 83.77; H 5.73; equiv. (by titration) 299.3, 302.8. $C_{21}H_{16}O_2$.
Calculated %: C 83.99; H 5.37; equiv. 300.3.

II. Condensation with Triphenylbrommethane in the Absence of Solvent. 18.5 g of diazoacetate was added dropwise with mechanical stirring to 52 g of triphenylbrommethane and 0.2 g of anhydrous copper sulfate, heated at 160-165°. 5.2 liters of nitrogen was evolved (19°, 759.2 mm), which exceeded the theoretically required amount by 22%. The excess was attributed to the presence of carbon dioxide in the nitrogen, which was qualitatively determined by the use of baryta water. The reaction product (bromacetate) possessed considerable lachrymatory properties. It did not crystallize upon standing in the cold. After distilling off the bromacetate in vacuo (b.p. 50-60° at 11 mm, yield 11 g or 81.2% of the theoretical), there was obtained from the residue a dark, resinous mass which crystallized from a mixture of benzene and petroleum ether. After repeated crystallizations from benzene, and then from alcohol, 18 g of 1,1,2-triphenylbutene-1 (V) resulted, with m.p. 91-92° (78% of the theoretical yield). On concentrating the benzene-petroleum mother liquor from hydrocarbon (V), about 1 g of diphenylindone (IV) resulted.

1,1,2-Triphenylbutene-1 (V). Colorless needle crystals (from alcohol), m.p. 91-92°. Poorly soluble in cold conc. H_2SO_4, with formation of a green color, changing upon heating into an intense yellow.

0.0916 g, 0.0998 g substance: 0.3127 g, 0.3402 g CO_2: 0.0551 g, 0.0594 g H_2O. 0.2989 g, 0.4060 g substance: 13.62 g, 19.00 g C_6H_6 : Δt 0.40, 0.78°. Found %: C 92.11, 92.96; H 6.73, 6.98; M 281.5, 295.3 $C_{22}H_{20}$. Calculated %: C 92.90; H 7.09; M 284.4.

* The diazoacetate was purified beforehand by steam distillation in vacuo.

Diphenylindone (IV). Crystals, ruby-red in color (from alcohol), m.p. 150°. Gave a green coloration with conc. H_2SO_4 in the cold; upon heating, an orange color. The melting point and other properties corresponded to those indicated in the literature [8].

Found %: C 89.19; H 4.87. $C_{21}H_{14}O$. Calculated %: C 89.33; H 4.96.

iii. Condensation with Diphenylbrommethane. 119.2 g of diphenylbrommethane [17] and 0.3 g of anhydrous $CuSO_4$ was heated to 80° and with mechanical stirring 55 g of diazoacetate was added to the mixture dropwise. 9.2 liters of nitrogen was evolved (17°, 764 mm). The hot reaction mixture was filtered off from the catalyst, and crystals of the crude ester (VII) separated out from the filtrate upon standing in a desiccator, m.p. 110°, weighing 50.1 g (31.2% of the theoretical yield). A considerable portion of the ester (VII) remained apparently in the mother liquor along with products of a resinous character (see below).

Ethyl β-Brom-α-phenylhydrocinnamate (VII). The crude sample was purified by crystallization from alcohol-benzene mixture. Colorless, light flaky crystals with m.p. 132°. Soluble in alcohol, benzene, ligroin, petroleum ether. Yield of pure sample was 32.3 g or 20.1% of theoretical.

0.1161 g, 0.1538 g substance: 0.0650 g, 0.0867 g AgBr. 0.1085 g, 0.3775 g substance; 17.06 g, 25.78 g C_6H_6: Δt 0.10, 0.24°. Found %: Br 23.82, 24.00; M 326.3, 346.8. $C_{11}H_{13}O_2Br$. Calculated %: Br 23.98; M 333.22.

Investigation of the Mother Liquor. Bromacetate. The mother liquor remaining after separation of the ester (VII) crystals possessed a sharp lachrymatory odor. As the result of vacuum fractional distillation, 14 g (17.2% of the theoretical yield) of bromacetate resulted with a m.p. of 155-162°, along with 20 g of resinous, non-distillable residue. After repeated distillations, the bromacetate possessed the following constants: b.p. 158-159° and n_D^{20} 1.451 [16]. The resinous residue was boiled with a solution of alcoholic alkali (42 g of KOH in 170 ml of alcohol); the resulting homogeneous solution, dark in color, was diluted with water and acidified with sulfuric acid. The resinous acids separated from the residue were purified by crystallization from alcohol with subsequent reprecipitation. 4.3 g of colorless crystals of pure α-phenylcinnamic acid (X) with m.p. 172° resulted. A sample mixed with known sample (X) (m.p. 172°), prepared by the action of the Na salt of phenylacetic acid upon benzaldehyde [13], did not show depression.

α-Phenylcinnamic Acid; A) Ester (VII) and Alcoholic Alkali. 2 g of ester (VII) was heated with 2 g of KOH solution in 50 ml of alcohol. The alcohol was distilled off in vacuo, the residue dissolved in 100 ml, and the solution acidified with dilute sulfuric acid. From the solution colorless crystals of the acid (X) precipitated out, with m.p. 169°. Yield – 1.3 g (96.6% of theoretical). After crystallization from benzene, m.p. was 171-172°. A sample mixed with authentic sample of Acid (X) prepared as indicated above, did not show depression.

B) Ester (VII) and Aqueous Alkali. Hydrolysis of 3.3 g of ester (VII) with 20 ml of 10% aqueous caustic potash by boiling, and subsequent acidification of the alkaline solution gave 2.15 g (96.8% of the theoretical yield) of acid (X), with m.p. 169°. After crystallization from benzene, m.p. was 171-182°.

In conformity with the literature data [13], the acid (X) discolored potassium permanganate solution, did not add bromine in chloroform, and sublimed. Below are given data on the analysis of acid (X), and of the silver salt derived from it.

Found: equiv. 223.1, 224.7; OH 1.059, 0.984. $C_{15}H_{12}O_2$. Calculated: equiv. 224.3; OH 1.0, 0.2982 g, 0.1591 g salt: 0.0979 g, 0.0527 g Ag. Found %: Ag 32.83, 33.12. $C_{15}H_{11}O_2Ag$. Calculated %: Ag 32.62.

C) Oxidation of Acid (X). 2 g of acid (X) was dissolved in soda and oxidized in the cold with 2% $KMnO_4$ (3.6g). After the usual treatment, the aqueous solution of oxidation products was concentrated and acidified with sulfuric acid. There resulted 1.25 g of benzoic acid with m.p. 120° (57.4% of theoretical yield); identified by the mixing test with known acid. There was isolated from the filtrate by ether extraction 0.9 g of crude benzoylformic acid in the form of a dark oil, which crystallized upon storage desiccator. After pressing out on a plate, and crystallizing from water, the crystals melted at 56-57°. Literature data: m.p. 65° [20]. Yield – 0.4 g (30% of theoretical). With conc. H_2SO_4 it gave a characteristic violet color [18]. Due to insufficiency of material, the acid was characterized in the form of its phenylhydrazone [19]. The m.p. of the phenylhydrazone, 153°, corresponds to the literature data [19]. A sample mixed with the phenylhydrazone of the same acid, obtained according to Glücksmann [20], did not show depression.

Dealkylation of Ester (VII): α-Phenyl-β-bromhydrocinnamic acid (XII). 1.5 g of ester (VII) and 30 ml of glacial acetic acid saturated with HBr at 0° were placed in a thick-walled tube. The tube was sealed in the cold and was then heated at 80° for 12 hours in an oil bath with thermostat. The acetic acid was removed in vacuo after completion of the experiment. In the residue there was 0.95 g (69.1% of the theoretical quantity) of crude, yellow-

colored acid (XII), which, after washing with ligroin and recrystallizing from chloroform-petroleum ether mixture (3:1), melted at 185° in conformity with the literature data [13]. For the comparison, known acid (XII) was obtained by the action of HBr in glacial acetic acid upon acid (X) which in its turn was synthesized according to directions given by the same author [13]. A mixed sample of the two specimens of acid (XII) melted without depression.

Found %: Br 26.07, 26.57. $C_{15}H_{13}O_2Br$. Calculated %: Br 26.18. Characteristic reaction: upon addition of an alcoholic solution of $AgNO_3$, AgBr precipitated, and from the filtrate, upon dilution, a flaky precipitate of stilbene separated (m.p. 124° [16].)

Synthesis of Ester (VII) from Known Acid (XII). 2 g of known acid (XII) and 50 ml of alcohol saturated with HCl were heated under reflux for 1 hour on a water bath. Concentration and subsequent cooling of the solution led to precipitation of colorless crystals of the ester (VII), with m.p. 129-130°. Yield – 2 g (93% of theoretical). After crystallization from alcohol, m.p. 131-132°. A sample mixed with ester (VII) obtained by condensation reaction melted at the same temperature.

IV. Condensation with Benzyl Bromide. 45 g of diazoacetate mixed with 40 g of benzyl bromide was added dropwise with stirring to 200 g of benzyl bromide and 0.5 g of copper powder, heated at 120°. 10.5 liters of nitrogen were evolved (21°, 768 mm). The reaction product was separated from catalyst by filtration and redistilled in vacuo. After distilling off the principal excess benzyl bromide (200 g, b.p. 82-85° at 14 mm), 8.2 g of a fraction with b.p. 93-96° at 14 mm was distilled off, which had an ethereal odor and was unsaturated with respect to $KMnO_4$. The content of this fraction was taken to be fumaric acid ester (according to the literature, b.p. is 98° at 14 mm) on the basis of having synthesized the diphenacylic ester, with m.p. 194.5°, from it by the earlier-described [2] method. The latter was identified with known diphenacylfumarate by the mixed sample test.

After removal of the fumarate, there remained in the distilling flask a viscous, resinous product of dark color, which was not distillable in a vacuum of 0.01 mm.

Investigation of the Non-Distillable Residue. The Hydrazide of Hydrocinnamic Acid. The ester of α-bromhydrocinnamic acid (XIII) was assumed to be present in the non-distillable residue, according to Equation (12). Because of the impossibility of separating the ester (XIII) from the residue, an attempt was made to convert it into cinnamic acid by the action of alcoholic alkali upon the entire resinous residue. Upon acidification of the alkaline solution, a viscous, dark-colored acid of semi-liquid consistency resulted, purification and characterization of which was unsuccessful. A second attempt consisted in a reductive dehalogenation of the residue [see Equation (13)].

20 g of zinc dust was gradually added to a mixture composed of 50 g of the resinous residue, 50 ml of 50% acetic acid, and 50 g of alcohol heated to 60°. After 1 hour of heating, the solution was separated from the zinc by filtration, the filtrate was diluted with water, and then neutralized with dry soda. The oily layer that separated was extracted with ether. After drying and distilling off the solvent, the oil was molecularly distilled in vacuo at 10^{-2} mm. It was possible to distill only a small portion of the product. Resulting fractions: I) b.p. 55-65°, n_D^{20} 1.4982-1.5000, 2.4 g; II) b.p. 65-75°, n_D^{20} 1.5056, 1 g; III) b.p. 85-95°, n_D^{20} 1.5240, 0.8 g; IV) b.p. 100-120°, n_D^{20} 1.5062. Results of the fractionation indicated the formation of quite a complex mixture of products. Only Fraction I was investigated, which was assumed to be the ethyl hydrocinnamate (XIV) on the basis of having derived from it the hydrazide (XV) with m.p. 99° according to the method of Jordan [21]. Because of insufficient amount of the substance, the hydrazide was purified by a single crystallization (from alcohol). The hydrazide of known hydrocinnamic acid (m.p. 48°) melted at 103° [21], and a mixed sample – at 100°.

SUMMARY

1. By condensing diazoacetate with di- and tri-phenylbrommethane in the presence of anhydrous copper sulfate, there can be obtained in one step, and with satisfactory yields, various compounds which are either not described in the literature, or which are not easily accessible for synthesis by other means.

2. Benzyl bromide in the presence of copper bronze also condenses with diazoacetate, but only in negligible yield. The observed increase in yield of condensation product in the series benzyl bromide-diphenylbrommethane-triphenylbrommethane may be related to the decrease in energy of the C-Br bond in this series.

3. Various transformations of certain substances have been investigated for the purpose of determining their structures and for explaining the mechanism of reaction between halogen derivatives of the hydrocarbons with diazoacetate in the presence of copper catalysts.

4. The conclusion postulated regarding the mechanism of the reactions for all three halogen derivatives of the aliphatic-aromatic series investigated here allows one to assume a single common mechanism of interaction as for that described earlier for the halogen derivatives of the aliphatic hydrocarbons.

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• See Consultants Bureau translation, p. 953.
•• See Consultants Bureau translation, p. 1393.
••• See Consultants Bureau translation, p. 63.

SULFONATION AND SULFONIC ACIDS OF ACIDOPHOBIC COMPOUNDS

XXI. SULFONATION OF 2,5-DIMETHYLTHIOPHENE. A COMPARISON OF THE SULFONATING ACTIONS OF PYRIDINE-SULFOTRIOXIDE, PYRIDINE-BIS-SULFOTRIOXIDE AND OF DIOXANE-SULFOTRIOXIDE

A. P. Terentyev and G. M. Kadatsky

In the works on sulfonation of various acidophobic compounds by one of us with his co-workers [1,2,3], various compounds of sulfuric anhydride were used: pyridine-sulfotrioxide ($Py \cdot SO_3$), pyridine-bis-sulfotrioxide ($Py \cdot S_2O_6$) and dioxane-sulfotrioxide ($D \cdot SO_3$). The actions of the first and second [1], and also of the first and third [2], were compared with thiophene and pyrrole derivatives. To compare their sulfonating actions on the same compounds, thiophene sulfonation was also carried out with $D \cdot SO_3$ and 2,5-dimethylthiophene with all three reagents.

On the basis of work carried out earlier on the sulfonation of pyrrole derivatives, it can be concluded that $D \cdot SO_3$ at room temperature and $Py \cdot SO_3$ at 100-120° possess the same sulfonating ability and give the same sulfoderivatives. It seemed that thiophene with $D \cdot SO_3$ should also produce the disulfoacids. However, the investigation carried out indicated that at room temperature thiophene is sulfonated to the monosulfo acid. Thus, $D \cdot SO_3$ is closer in its properties to $Py \cdot S_2O_6$ than the monosulfonating thiophene under the same conditions. with the use of two reagents, yields of the same order resulted – 75 and 86% respectively.

A test of the action of three reagents on 2,5-dimethylthiophene has also indicated that $Py \cdot S_2O_6$ and $D \cdot SO_3$ react similarly, and give 2,5-dimethylthiophenylsulfonic-3-acid in almost theoretical yield – up to 95%. $Py \cdot SO_3$ even at 135° gives considerably lower yield of monosulfo acid (47%, calculated according to substance taken; 75% calculating on the basis of thioxene entered into reaction).

Interaction of $Py \cdot SO_3$ and thioxene showed a depressed activity for the latter as compared with thiophene, which under these conditions gave the disulfoacid in good yield. This result indicates: distinction between the α- and β-positions of the thiophene ring. Even when activated by methyl groups, the β-positions are considerably less reactive. This reaction also shows that 2,5-dimethylthiophene, with reference to its activity, is placed between thiophene and benzene, somewhat closer to the latter.

In one of the preceding articles [1], the possibility of direct synthesis of the sulfochloride from the pyridine salt which resulted from interaction of thiophene with $Py \cdot S_2O_6$ was demonstrated. In the present work, the 2,4-dimethylthiophenylsulfochloride synthesized by the same method, and without separating, was converted to the sulfamide with a total yield of 44 %.

In using $D \cdot SO_3$, the authors have taken approximately a double excess of dioxane in the sulfonation reaction. It is possible that the use of other ratios for dioxane and sulfuric anhydride will produce a sulfonating agent with somewhat different properties.

It is necessary to mention that the direct monosulfonation of 2,5-dimethylthiophene has been realized for the first time, by the authors. L. Keiser [4] obtained the monosulfo acid by an indirect method – by dehalogenation of 4-brom-2,5-dimethylthiophenylsulfonic-3-acid, obtained by the action of sulfuric acid on bromthioxene. W. Steinkopf, H. Jacob and H. Penz [5] obtained the anhydride of the disulfoacid in 50% yield by sulfonation of thioxene with 33% oleum.

EXPERIMENTAL

Thiophene was obtained by interacting sodium succinate with phosphorus pentasulfide [6]; 2,5-dimethylthiophene – by heating acetonylacetone; 2,5-dimethylfurane by hydrolysis with phosphorus trisulfide [7].

Sulfonation of 2,5-Dimethylthiophene

1. With Pyridinesulfotrioxide. 4 g of thioxene, 5.7 g of $Py \cdot SO_3$ and 6 ml of dichlorethane were heated at 130° in a sealed tube to complete fusion of $Py \cdot SO_3$ (8 hours). The cooled, light-brown sulfo mass was treated with water. The water layer was heated with an excess of barium carbonate for complete removal of pyridine and water vapor. After filtration, the aqueous solution was evaporated to a small volume and the salt was precipitated with alcohol; yield 4.55 g (46.6%). From the dichlorethane layer, by mercurization, was isolated 1.5 g of thioxene which did not enter into the reaction. The yield of salt, calculated on the basis of thioxene which entered into reaction, was 74.6%.

2. With Pyridine-bis-sulfotrioxide. 1.12 g of thioxene was added to $Py \cdot S_2O_6$, prepared from 1.6 g of $Py \cdot SO_3$ and 0.8 g of sulfuric anhydride in 8 ml of dichlorethane. After 24 hours the greenish reaction mass was treated with an excess of an aqueous suspension of barium carbonate, with heating. After the usual separation, 2.6 g (93.8%) of barium 2,5-dimethylthiophenylsulfonate-3 resulted.

3. With Dioxanesulfotrioxide. 3.36 g of thioxene was added to the $D \cdot SO_3$ solution prepared from 4.8 g of sulfuric anhydride and 10 ml of dioxane in 48 ml of dichlorethane. After standing for 24 hours, the dark-colored reaction mass, from which at times dioxanesulfonate crystals precipitated, was treated as usual. 7.8 g (95.1%) of the barium salt resulted.

Barium 2,5- dimethylthiophenesulfonate – white lustrous scales, readily soluble in water.

3.068 mg substance: 1.321 mg $BaSO_4$. 7.792 mg substance: 3.345 mg $BaSO_4$. 3.390 mg substance: 1.481 mg $BaSO_4$. Found %: Ba 25.34, 25.26, 25.71. $C_{12}H_{14}O_6S_4Ba$. Calculated %: Ba 25.54.

The S-(α-naphthylmethyl)-thiouronic salt of 2,5-dimethylthiophenesulfonic-3 acid was obtained by the interaction of equivalent quantities of saturated aqueous solutions of naphthylmethylthiouronium chloride and the barium salt of thioxenesulfoacid. The resulting precipitate was recrystallized from aqueous alcohol, m.p. 195°.

4.840 mg substance: 0.304 ml N_2 (26°, 745 mm). Found %: N 6.80. $C_{13}H_{20}O_3N_2S_3$. Calculated %: N 6.87.

2,5-Dimethylthiophenesulfamide-3. To $Py \cdot S_2O_6$ prepared from 4.8 g of $Py \cdot SO_3$ and 2.4 g of sulfuric anhydride in 24 ml of dichlorethane, 3.36 g of thioxene was added. 6.3 g of phosphorus pentachloride was added after a period of 72 hours. After 3 hours the mixture was poured onto ice, and the dichlorethane layer separated. A concentrated solution of ammonia was added to it, the mixture concentrated on a water bath, and the residue reprocessed with ammonia and concentrated by evaporation.

The dry residue was placed in a glass tube, one end of which was pulled out to a capillary. This microflask extractor was suspended by a thin wire to a reflux condenser connected to a round-bottomed flask containing ether. The flask with the microextractor was placed in warm water and the sulfamide extracted by the ether flowing down from the condenser. The yield of amide was 2.2 g (44%), m.p. 141-142°. Literature data: m.p. 135° [4].

Sulfonation of Thiophene with Dioxanesulfotrioxide. 3 g of sulfuric anhydride dissolved in 30 ml of dichlorethane was added to 5 ml of dioxane with ice-water cooling and stirring, followed by 3.1 g of thiophene. After standing for three days and nights, the liquid, green in color, containing the dioxane salt crystals, was treated with water. 6.4 g of barium thiophenesulfonate-2 resulted from the aqueous solution by the usual procedure. Yield was about 75% calculated on the basis of thiophene taken.

SUMMARY

A comparison of the sulfonating actions of pyridinesulfotrioxide, pyridine-bisulfotrioxide and dioxanesulfotrioxide, with the examples of thiophene and 2,5-dimethylthiophene sulfonation, have been carried out in this work. It has been demonstrated that the last two reagents are similar in action. They sulfonate thiophene with 86 and 75% yields, and 2,5-dimethylthiophene with 94 and 95%, respectively, producing the monosulfo derivatives. Pyridinesulfotrioxide at 130° also gives the monosulfo acid of 2,5-dimethylthiophene, but with 75% yield, calculated on the basis of thioxene that entered into reaction.

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THE SULFONATION REACTION

XXVI. DETERMINATION OF SOME DI- AND TRI-SULFOACIDS OF NAPHTHALENE

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The authors at an earlier date [1] developed a method for the quantitative determination of 1,5-, 2,6- and 2,7-disulfoacids of naphthalene in sulfonation mixtures which do not contain the monosulfoacids of naphthalene. A brief review of the literature on analysis of disulfo mixtures was given in the work mentioned. The foundation of the present work on analysis of naphthalene disulfoacids is the method of exhaustive sulfonation. This method was proposed for the first time by V. N. Ufimtsev and A. F. Krivoshlykova [2] who, after sulfonation with oleum, nitrated the mixture and then reduced the nitrogroups, and diazotized the aminosulfoacid. Thus, the relative quantities of 1,6- and 1,7-naphthalenedisulfoacids were determined, but the method was not tested on artificial mixtures in the presence of other isomers, and the degree of its accuracy is apparently not high. Lantz [3] likewise used essentially the same method, after sulfonation, nitrating the mixture in the cold and with heating. However, this method was tested by Lantz without the presence of 1,7- and 1,3-isomers, and requires large corrections which are experimentally found for each determination, which makes it unreliable.

Upon exhaustive sulfonation with oleum, 1,5-, 1,7- and 2,6-naphthalenedisulfo acids convert into 1,3,5,7-tetrasulfoacid, and the 1,3- and 2,7-disulfoacids into 1,3,6-trisulfoacid. As shown below, the 1,3-disulfo acid sulfonates to the extent of 75% into 1,3,5,7-tetrasulfoacid.

In addition to the exhaustive sulfonation, as a basis of the method is observation that 1,3,5,7-naphthalenetetrasulfochloride is almost completely insoluble in benzene, while 1,3,6-naphthalenetrisulfochloride dissolves in the amount of 10.7 g per 100 g of solution [4]. Therefore, the disulfoacid mixture is sulfonated with oleum, and then chlorsulfonic acid is added to the mixture to convert the sulfo acids into the chlorides. The mixture is poured onto ice, the chlorides are filtered off, dried, weighed, and then treated on the filter with benzene. After weighing the tetrachloride residue, the ratio of disulfoacids sulfonating to tri- and tetra-derivatives is determined.

In combination with the earlier developed method [1] for the determination of 1,5-, 2,7- and 2,6-isomers, the exhaustive sulfonation method permits determination of the 1,6-isomer, and by difference the 1,7-isomer, also, in the absence of 1,3-disulfoacid in the mixture. With a small amount of the latter, its sum with the 1,7- isomer is determined with some error.

The method described above also permits determination of the 1,3,6-trisulfoacid and the sum total of 1,3,5- and 1,3,7-trisulfoacids in a mixture containing trisulfoacids of naphthalene.

EXPERIMENTAL

The tri- and tetra-sulfoacids are not completely converted into the chlorides by the action of chlorsulfonic acid; therefore, the first prerequisite is to demonstrate that tri- and tetra-chlorides are formed in the same ratios in which the tri- and tetra-sulfoacids are present in the mixture at the start.

A weighed portion of 1,3,6-naphthalenetrisulfochloride, m.p. 198.5°, was mixed with a weighed portion of 1,3,5,7-tetrachloride, m.p. 272°. The chlorides were dissolved in mixtures of variable composition of chlorsulfonic and sulfuric acids, the solution was heated for 2 hours at 125°, and then was poured on ice. The chlorides were filtered off, washed, dried and weighed. The 1,3,6-trichloride was then washed with benzene on the filter, and from the tetrachloride residue the ratio with chlorides was determined. The experimental results, given in Table 1, indicate that the sulfoacids convert into the chlorides, and in the same ratios in which they are present dissolved in a mixture of chlorsulfonic and sulfuric acids.

TABLE 1

Isolation of the Chlorides from a Solution Containing a Mixture of Chlorsulfonic and Sulfuric Acids.

Expt. No.	Taken (in %)		Found (in %)	
	1,3,6-trichloride	1,3,5,7-tetrachloride	trichloride	tetrachloride
219	10.6	89.4	11.1	88.9
226	50.5	49.5	51.2	48.8
225	58.5	41.5	59.0	41.0
224	81.0	19.0	81.6	18.4

The procedure was then developed for sulfonation experiments on disulfochloride

mixtures. A weighed portion of the pure disulfochlorides was placed in a test tube and 3 ml of 55-65% oleum was added, about 1 g in total weight. The test tube was sealed and heated at a temperature of 160-162° for 2-3 hours. The tube was then opened and 5 ml of chlorsulfonic acid was added and the mixture again heated at 120-125° for 2 hours to convert the sulfoacids into the chlorides. The mixture was then poured onto ice, the chlorides filtered off, washed with water, dried, weighed, washed with benzene, and the residue again weighed.

The experimental results given in Table 2 indicate that the deviation after conversion of the tetrachloride to the dichloride does not exceed 1%. At the same time, the 1,3-disulfochloride forms 75% of the tetrasulfoacid and 25% of the trisulfoacid. The tetrachloride was obtained with somewhat lower melting point than the pure product (Table 2).

TABLE 2

Exhaustive Sulfonation of Naphthalenedisulfochloride at a Temperature of 160-162°

Experiment No.	Dichloride taken (in % of the total weighed portion)						Tetrachloride found by conversion to dichloride (%)	Difference (in %)	Melting point of the tetrachloride
	1,3-	1,5-	1,6-	1,7-	2,6-	2,7-			
252	100						76.8		252°
246	100						74.5		249
251			51.7	48.3			51.2	0.5	250
228					30.6	69.4	29.8	0.8	252
233					94.2	5.8	94.2	0	261
245		9.6	90.4				9.2	0.4	
248		10.1	89.9				10.2	0.1	
204		29.4	70.6				28.4	1.0	255
239		31.3	68.7				31.1	0.2	
205		44.6	55.4				44.8	0.2	252
247		50.2	49.8				51.0	0.8	
250		78.7	21.3				77.9	0.8	254
236		79.3	20.7				78.6	0.7	258
214		93.4	6.6				93.7	0.3	254

Finally, the method was tested on artificial mixtures of the pure disulfoacids of naphthalene. To a weighed portion of about 1 g of the disulfoacid mixture, containing a known quantity of water of hydration, 2 to 2.3 g of the monohydrate of sulfuric acid was added. The mixture thus resulted in an H_2SO_4 concentration of 86-90%, approximating that resulting from sulfonation of naphthalene to the disulfo stage with the monohydrate of 98% H_2SO_4. 5-7 ml of oleum was added to the mixture and the sulfo mass was heated for 2 hours at 160° in a sealed test tube. The sulfo acids were then converted to the chlorides by heating with 15 ml of chlorsulfonic acid. Further steps are described above. The experimental results given in Table 3 indicate that with the sulfo acid mixture the determination errors again usually do not exceed 1%

Determination. About 3 g of the sulfo mass (weighed on technical scales) with a content of about 1 g of disulfoacids is placed in a test tube and ½ ml of 65% oleum added. The test tube is sealed and placed in a safety iron tube with screw top through a socket in which is passed a thermometer and the tube is placed in an Eijkman apparatus. After heating at 161-163° for 2 hours with boiling butyric acid in the outer container of the Eijkman apparatus, the test tube is unsealed, 15 ml of chlorsulfonic acid added to the sulfo mass, and the mixture heated to 120-125° for one hour. The mass is then poured onto pure ice; the chlorides which result in the amount of about 0.5-0.6 g are filtered off, washed with water, dried, weighed, washed about six times with benzene, taking 5 ml portions for each washing, and the residue then weighed again. 2-3 drops of the filtrate from the last washing with benzene is evaporated on a watch glass. If a residue is not evident, then the washing is terminated. Before pouring the mass onto ice it is necessary to see that tetrachloride precipitate not separate from the reaction mixture. This distorts the results. In such case the mixture is heated anew to the dissolution of the precipitate, and, if necessary, chlorsulfonic acid is added and the mixture then poured while warm onto the ice.

The % of disulfoacids sulfonating to the tetrasulfoacid is determined by the formula:

$$\%\,(1,5\text{-},\ 1,7\text{-},\ 2,6\text{-acid}) = \frac{430}{5.3\frac{a}{b} - 1},$$

TABLE 3

Exhaustive Sulfonation of Naphthalenedisulfoacids at 160° for 2 hours.

Experiment No.	Disulfoacids taken (in % of total weighed batch)						Oleum taken (in ml)	Tetrachloride found by conversion to disulfoacid (%)	Difference (in %)	Melting point of the tetrachloride
	1,3-	1,5-	1,6-	1,7-	2,6-	2,7-				
256		63.3	36.7				5	63.2	0.1	250°
257		58.2	41.8				5	58.5	0.3	258
273					27.8	72.2	6	27.4	0.4	
275			21.8	9.8	26.4	42.0	7	35.5	0.7	250
276			17.3	14.3	24.2	44.2	7	39.0	0.5	245
264		48.7	23.5	10.0	–	17.8	6	58.1	0.6	255
268		58.7	20.7	11.0	–	9.6	6	69.6	0.1	259
259	17.5	41.2	23.7	10.5	–	7.1	6	65.0	0.2•	249
265	16.3	40.5	23.9	9.4	–	9.9	6	61.6	0.5•	257

• It is considered that 1,3-disulfoacid converts to the extent of 75% into tetrasulfoacid and 25% into trisulfoacid.

where a = weight of tri- and tetra-chloride mixture, b = weight of tetrachloride.

Together with the earlier-described [1] method for determination of 1,5-, 2,6-, and 2,7-disulfoacids, the present method permits a complete analysis of the disulfomixtures resulting at low temperature, in the absence of 1,3- and 2,6-disulfoacids. These methods applied to disulfomixtures obtained at a temperature of about 130° cannot give accurate results since in such a mixture a considerable quantity of 1,3-disulfoacid will be present, which does not sulfonate completely to the tetrasulfoacid. Both methods are applicable to sulfo mixtures obtained at high temperatures (150-180°); since with a complete absence of the 1,5-disulfoacid the mixture is composed primarily of 2,6- and 2,7-isomers, and the 1,3-acid content in the presence of 1,6- and 1,7-isomers is also negligible. In such mixtures it is possible to determine 2,6-, 2,7- and 1,6- and the sum of 1,7- and 1,3-isomers. This method is also applicable, with equal success, to an analysis of naphthalene trisulfoacid mixtures. At the same time the content of 1,3,6-trisulfoacid and the sum of 1,3,5- and 1,3,7-trisulfoacids can be determined.

The following products were used by the authors in their work: 1,5-naphthalenedisulfochloride, m.p. 184°; 1,3-dichloride, m.p. 137°; 1,7-dichloride, m.p. 122°; 1,6-dichloride, m.p. 129°; 2,6-dichloride, m.p. 226°, and 2,7-dichloride with an m.p. of 162°. Free disulfoacids resulted in which the content of water of crystallization was determined alkalimetrically by saponification of the chlorides with water-alcohol mixture, and the solution evaporated to dryness on a water bath. Distilled chlorsulfonic acid and pure oleum were used.

SUMMARY

A method for the quantitative determination of two naphthalenedisulfoacid groups (sulfonating to the tetrasulfoacid and to the trisulfoacid) has been developed by the method of exhaustive sulfonation, conversion of the polysulfoacids into the chloranhydrides, and separation of the latter by treatment with benzene.

The method is applicable to the analysis of naphthalenesulfoacid mixtures. The error in determination of the isomers does not exceed 1% by the method described.

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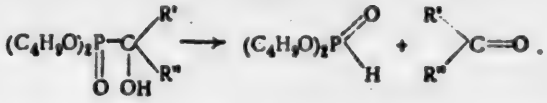
• See Consultants Bureau English translation page 1663.
•• See Consultants Bureau English translation page 2091.

INTERACTION OF DIALKYLPHOSPHOROUS ACIDS WITH ALDEHYDES AND KETONES

IV. BUTYL AND ALLYL ESTERS OF α-HYDROXYALKYLPHOSPHINIC ACIDS

V. S. Abramov, R. V. Dmitrieva and A. S. Kapustina

The butyl and allyl esters of various α-hydroxyalkylphosphinic acids are described in the present article. The esters were obtained by methods described in the preceding articles [1] by the authors – by reacting dibutylphosphorous and diallylphosphorous acids with various aldehydes and ketones in the presence of freshly-prepared sodium methylate. The reaction proceeds rapidly. The reaction products can be immediately fractionally distilled. Upon interaction of dibutylphosphorous acid with methylpropylketone, diethylketone and with dibenzylketone, there is a temperature rise of from 15° to 27°. Such a rise in temperature undoubtedly indicates progress in the reaction and formation of the butyl esters of the corresponding α-hydroxyalkylphosphinic acids. However, upon fractionally distilling the reaction products, it appeared impossible to separate the butyl ester of α-hydroxyalkylphosphinic acid. During fractional distillation dibutylphosphorous acid distilled off slowly. More rapid and intense heating during the fractional distillation led to violent decomposition. The authors consider that during the fractional distillation, there occurs a gradual decomposition of the butyl ester of α-hydroxyalkylphosphinic acid:



Dibutylphosphorous acid distills off as it forms. The ketones present – methylpropylketone and diethylketone – are removed in vacuo without condensation, dibenzylketone being recovered completely from the reaction.

Upon interacting dibutylphosphorous acid with isovaleric aldehyde, the reaction mass temperature rose from 20° to 104° and the butyl ester of α-hydroxy-γ-methylbutylphosphinic acid was no doubt formed. The ester was isolated, but upon its fractional distillation, partial decomposition occurred. The acid formed was added to the ester and increased the phosphorous content. From the resulting partial decomposition may be explained the high phosphorous content as compared with theory.

Upon interacting diallylphosphorous acid with isovaleric and with benzoic aldehydes, the temperature of the reaction mass rose with reaction from 23° to 45°, and with the benzoic, from 20° to 98°. Allyl ester of α-hydroxyalkylphosphinic acids were formed. However, esters were not obtained in the pure state since gradual decomposition occurred during their fractional distillation. It was even possible to partially redistill the allyl ester of α-hydroxybenzylphosphinic acid, but at the same time it contained a large quantity of decomposition products. The residue polymerized to a hard mass with violent decomposition. A similar picture resulted from the interaction of diallylphosphorous acid with methylethylketone and acetophenone. From the heat evolved during the course of the reaction, it should be considered that the allyl esters of the corresponding α-hydroxyalkylphosphinic acids are produced; however, they failed to separate.

An interesting case is that of interaction between dibutylphosphorous acid and the ethyl ester of 2-ketocyclopentanecarboxylic acid. If dibutylphosphorous acid reacts vigorously with cyclopentanone and with cyclohexanone with large heat evolution and with formation of the butyl esters of α-hydroxycyclopentylphosphinic and α-hydroxycyclohexylphosphinic acids, then the presence of a carbon atom of the carbethoxyl group adjacent to the carbonyl group eliminates the reaction. Here the effect of the carbethoxyl group is evident.

EXPERIMENTAL

The experiments were carried out in the same manner as described in the preceding articles, a few drops of freshly-prepared sodium methylate being added to an equimolecular mixture of the dibutylphosphorous or diallylphosphorous acid and the aldehyde or the ketone. After standing, or upon heating in some cases, the reaction products were fractionally distilled in vacuo. Data for the resulting butyl and allyl esters of the various α-hydroxyalkylphosphinic acids are given in Tables 1 and 2.

TABLE 1
n-Butyl Esters of α-Hydroxyalkylphosphinic Acids

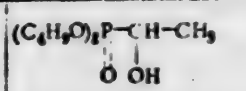
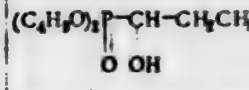
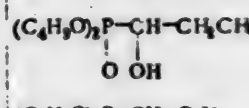
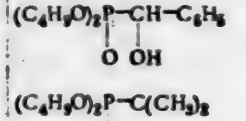
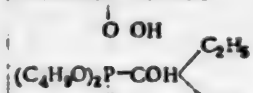
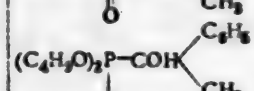
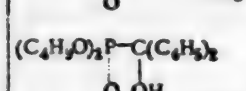
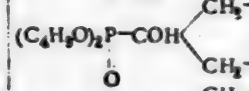
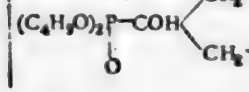
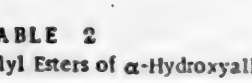
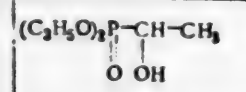
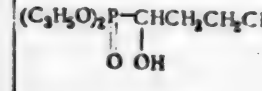
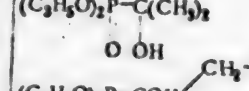
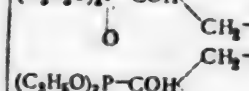
No.	Formula for the ester obtained	Boiling point	d_4^{20}	n_D^{20}	MR_D Calculated	MR_D Found	Ester yield (%)	Phosphorous content (in %) Calculated	Phosphorous content (in %) Found
1		162-163° (9 mm)	1.024	1.4384	60.26	61.08	56.7	13.03	13.25; 13.35
2		168-170° (6 mm)	1.000	1.4400	69.49	70.06	49.0	11.65	11.90; 11.84
3		180-182° (11 mm)	0.998	1.4360	74.11	73.42	–	11.07	14.08; 14.20
4		168-170° (5 mm)	1.026	1.4680	79.75	81.28	–	10.33	10.02; 10.87
5		154-155° (7 mm)	1.018	1.4366	64.88	64.81	59.2	12.30	12.53; 12.34
6		156-157° (8 mm)	1.015	1.4403	69.49	69.16	57.7	11.65	11.53; 11.72
7		179-180° (9 mm)	1.025	1.4670	84.37	84.99	30.0	9.87	10.05; 10.07
8		207-208° (7 mm)	1.030	1.4760	103.85	102.93	–	8.24	9.17; 9.03
9		178-180° (9 mm)	1.049	1.4549	71.92	71.87	40.4	11.15	11.34; 11.22
10		178-180° (7 mm)	1.039	1.4570	76.53	76.53	48.7	10.62	10.91; 10.98

TABLE 2
Allyl Esters of α-Hydroxyalkylphosphinic Acids

No.	Formula for the ester obtained	Boiling point	d_4^{20}	n_D^{20}	MR_D Calculated	MR_D Found	Ester yield (%)	Phosphorous content (in %) Calculated	Phosphorous content (in %) Found
1		151° (10 mm)	1.1187	1.4565	49.99	50.09	65.3	15.05	14.53; 14.92
2		163-164° (10 mm)	1.0769	1.4552	59.33	58.98	31.6	13.25	13.22; 13.28
3		132° (12 mm)	1.0907	1.4500	50.03	50.24	38.8	14.06	14.08; 14.19
4		165-167° (7 mm)	1.1253	1.4740	61.74	61.47	45.7	12.60	11.94; 11.97
5		m.p. 56.5-57°	–	–	–	–	67.7	11.92	12.03; 11.90

Interaction of Dibutylphosphorous Acid with Methylpropylketone, Diethylketone and Dibenzylketone. 9.7 g (0.05 mole) of dibutylphosphorous acid and equimolecular quantities of the following were taken for reaction, respectively: 4.3 g of methylpropylketone, 4.3 g of diethylketone and 9.1 g of dibenzylketone. A few drops of freshly-prepared sodium methylate was added to each mixture. The reaction mass temperature upon addition of the sodium methylate increased from 20° to 37° in the reaction of dibutylphosphorous acid with methylpropylketone, from 17° to 33° in the reaction with diethylketone, and from 21° to 48° in the reaction with dibenzylketone.

The reaction products were heated on a paraffin bath at 120° to 130° for a prolonged period of time. Upon fractional distillation the initial substances in all cases were recovered with small losses.

Interaction of Dibutylphosphorous Acid with the Ethyl Ester of 2-Ketocyclopentanecarboxylic Acid. 9.7 g of dibutylphosphorous acid and 7.8 g of the ethyl ester of 2-ketocyclopentanecarboxylic acid were taken for reaction. The temperature of the reaction mass rose from 20° to 23° upon addition of the sodium methylate. The reaction mass was heated on a paraffin bath at 140-150° for a prolonged period. During fractional distillation in vacuo, the fractions obtained were: 3.6 g of the ethyl ester of 2-ketocyclopentanecarboxylic acid and 4 g of dibutylphosphorous acid. The residue — a non-distillable resinous mass.

Interaction of Diallylphosphorous Acid with Isovaleric Aldehyde. 8.1 g of diallylphosphorous acid and 4.5 g of isovaleric aldehyde were taken for reaction. The temperature of the reaction mass rose from 23° to 45° upon addition of freshly-prepared sodium methylate to the mixture. During fractional distillation of the reaction product, the initial substances were distilled off. The allyl ester of α-hydroxy-γ-methylbutylphosphinic acid was not obtained.

Interaction of Diallylphosphorous Acid with Benzoic Aldehyde. 8.1 g of diallylphosphorous acid and 5.3 g of benzaldehyde were taken for reaction. Several drops of freshly-prepared sodium methylate was added to the mixture. The temperature of the reaction mass rose from 20° to 98°. The product was then fractionally distilled in vacuo. Fractionation was carried out at 8 mm of final pressure with partial decomposition. At 170° violent decomposition occurred with formation of a light, foamy, hard product. During repeated distillations of the product which distilled during the first fractionation, up to 170°, violent decomposition was again repeated with the same picture of hard foam formation. The allyl ester of α-hydroxybenzylphosphinic acid did not result.

Interaction of Diallylphosphorous Acid with Methylethyl ketone and with Acetophenone. 8.1 g of diallylphosphorous acid and 4 g of methylethyl ketone or 6 g of acetophenone, were taken for reaction. Upon addition of sodium methylate to the reaction mass, the reaction temperature rose from 23° to 44° in the reaction with methylethyl ketone, and in the reaction with acetophenone — from 23° to 62°. The allyl esters of the corresponding α-hydroxyalkylphosphinic acids did not result upon fractional distillation of the reaction products. The initial products were recovered.

SUMMARY

1. Dibutylphosphorous acid and diallylphosphorous acid in the presence of sodium methylate reacts with aldehydes and ketones to give esters of α-hydroxyalkylphosphinic acids. Ten butyl esters of various α-hydroxyalkylphosphinic acids and five allyl esters of various α-hydroxyalkylphosphinic acids have been obtained.

2. Dibutylphosphorous acid and diallylphosphorous acid react with a whole series of other aldehydes and ketones; however, the esters of the corresponding α-hydroxyalkylphosphinic acids fail to separate. Upon fractional distillation decomposition to the original substances takes place. The decomposition process proceeds more rapidly the greater the radical size of the dialkylphosphorous acid.

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* See Consultants Bureau English translation, page 701.

THE SYNTHESIS AND PROPERTIES OF VINYLPHOSPHINIC ESTERS

I. THE PHOSPHONETHYLATION REACTION. ADDITION OF DIALKYLPHOSPHOROUS ACIDS, AMMONIA AND AMINES TO THE ETHYL ESTER OF VINYLPHOSPHINIC ACID.

A. N. Pudovik and G. M. Denisova

In a series of works completed by one of us and published in this journal over the past two years, a new method for the synthesis of various ester derivatives of phosphinic acids was developed, which consists of adding dialkylphosphorous acids to unsaturated electrophilic reagents: unsaturated ketones, aldehydes, nitriles, acids and their esters, and esters of the vinyl alcohols [1]. With the help of this method, a number of unknown esters of ketophosphinic, hydroxyphosphinic and cyanphosphinic acids, as well as esters of the phosophocarboxylic acids, and others, have been synthesized. As has already been mentioned, it is a very simple method in procedure, the initial components are readily accessible, and in a majority of the cases leads to the formation of phosphinic acid esters in good yield.

To develop and to expand this investigation, the authors have decided in the present work to investigate the possibility of using addition reactions between an electrophilic reagent and esters of vinylphosphinic acid. Esters of vinylphosphinic acid and the homologs have not been used up to the present time for addition reactions, and it should be mentioned in general that this interesting group of organophosphorous compounds has as yet received but little study. The literature contains a description for the satisfactory synthesis of only the simplest representative of the unsaturated phosphinic ester series — namely, that of the ethyl ester of vinylphosphinic acid [2], which has also been used by the authors. The vinylphosphinates have been found to be readily obtainable, and, which is equally important, they are adequately stable, do not polymerize upon prolonged storage at room temperature or during the process of vacuum fractional distillation or when heated for several hours on a water bath.

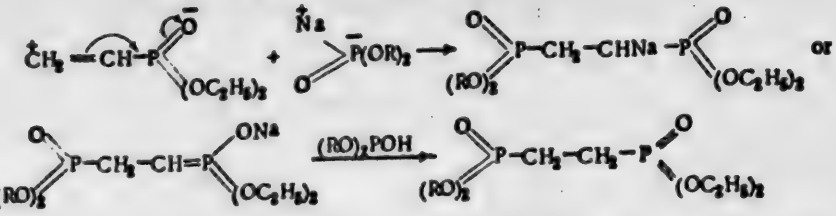
The first experiments carried out with vinylphosphinates indicated that they are sufficiently reactive to allow dialkylphosphorous acids to add to them in the presence of alcoholates of alkali metals. Since the reaction of addition to unsaturated phosphinates has received no study at all up to the present time, it was of interest therefore, to attempt their addition to other nucleophilic reagents usually used for similar purposes, in addition to the dialkylphosphorous acids. Preliminary experiments carried out along these lines have shown that ammonia, amines, malonic, cyanacetic and acetoacetic esters and their homologs, and also certain other reagents with mobile hydrogen atoms, add easily and rapidly to vinylphosphinate in the presence of alkali metal alcoholates, and in some cases without. Thus, this new reaction of nucleophilic reagent addition to vinylphosphinate which has been discovered by the authors, apart from its theoretical interest, may also prove to be of practical import for the synthesis of various phosphinate derivatives.

For convenience, and in order to reflect the basic nature of the process, it has been considered expedient to call this reaction which the authors have newly discovered "the phosphonethylation reaction", by analogy with the known and now widely-used cyanethylation reaction, by the use of which phosphonethylation reaction the phosphonethyl group can be introduced into various organic compounds. In the present article the authors have described addition to vinylphosphinate of dialkylphosphorous acids, of ammonia, and of some amines, for the most part secondary.

Addition of dialkylphosphorous acids to vinylphosphinate was carried out by the authors in the presence of alkali metal alcoholates. To avoid exchange of radicals between the alcoholates and the dialkylphosphorous acids, alcoholates with the same radicals as were contained in the dialkylphosphorous acids being added were used in the reactions. Reaction proceeded rapidly and was accompanied by strong heat evolution from the reaction mixtures. Yields of the addition products for the lower dialkylphosphorous acids constituted about 60% of the theoretical. The resulting esters of di-(dialkylphosphon)-ethane were viscous, colorless liquids, readily soluble in water, combining with alcohol and with ether in all proportions. The product obtained by addition of diethylphosphorous acid to vinylphosphinate was found to be identical with 1,2-di-(diethylphosphon)-ethane synthesized according to Ford-Moore [3] by reaction of triethylphosphite with ethylene bromide. Constants

for the latter product are: b.p. 167° (1 mm); $n_D^{16.5}$ 1.4425; as obtained by the authors from the addition reaction, 1,2-di-(diethylphosphon)-ethane had a b.p. of 164-165° (2 mm); n_D^{20} 1.4410; d_4^{20} 1.1376. The mechanism of the addition reaction may be expressed by the following general scheme:

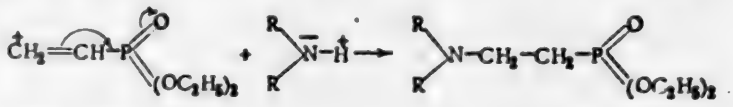
$$(RO)_2POH + RONa \rightleftharpoons (RO)_2PONa + ROH$$



The authors proceeded to investigate addition reactions of ammonia and amines to vinylphosphinate. The first experiments which involved the addition of ammonia to vinylphosphinate were carried out in aqueous and in alcoholic solutions at room temperature, without catalyst, and did not lead to positive results. Only by conducting the reaction in alcoholic solution, and in the presence of a small quantity of methyl alcoholate, did the reaction proceed successfully, leading to a 67.3% yield of β-diethylphosphonethylamine; b.p. 93-95° (4 mm); n_D^{20} 1.4270; d_4^{20} 1.0515. The ethylaminophosphinic acid itself was earlier synthesized by rather complex methods; by Finkelstein — from the ethyl ester of β-diethylphosphonpropionic acid [4], and by Kosolapoff [5] — by interaction of β-bromethylphthalimide and triethylphosphite with subsequent saponification of the reaction product. Incidentally, it should be mentioned that with few exceptions very little is known at present about the aminophosphinates and their derivatives. Recently, M.I. Kabachnik and his co-workers [6] obtained aminomethylphosphinic acid and some of its derivatives, utilizing the reaction between the ester of chlormethylphosphinic acid and ammonia.

With further investigation of the addition reaction of secondary amines to vinylphosphinate, there was observed the exceptional ease with which the lower aliphatic secondary amines added. The addition of dimethylamine to vinylphosphinate occurred immediately upon combining with one another, while at the same time the reaction mixture temperature rose to +55°. After standing for 24 hours at room temperature, the yield of addition product — β-diethylphosphonethyldimethylamine — constituted 83%. The β-diethylphosphonethyldimethylamine was confirmed by its synthesis from β-bromethylphosphinic ester and dimethylamine. The constants for the two products were found to be identical. The addition of piperidine to the vinylphosphinic ester proceeded somewhat less vigorously. After combining the reagents, the temperature of the reaction mixture had risen to 40°, 20 minutes after start of the experiment. Reaction proceeded without the need for any special catalyst, and after 24 hours standing at room temperature, the reaction product was obtained in a yield of 52.6%. The addition of aniline to the vinylphosphinic ester was attainable only in the presence of catalyst — sodium methylate; and the reaction did not go very smoothly. Along with the addition product — β-diethylphosphonethylaniline, which resulted only in negligible yield — a large quantity of low-boiling fraction was obtained.

The addition of amines to the vinylphosphinic ester may be represented by the following scheme:



where R = H, CH_3, C_6H_5, and other groups.

Results of reaction with diphenylamine were unsatisfactory; addition proceeded quite vigorously in the presence of sodium ethylate, but the addition product failed to separate since it failed to crystallize upon standing, and decomposed with attempts at distillation in high vacuum.

EXPERIMENTAL

Addition of Dimethylphosphorous Acid to Vinylphosphinic Ester. Saturated sodium methylate solution in methyl alcohol was added dropwise to the reaction mixture, which consisted of 8.2 g of vinylphosphinic ester and 5.5 g of dimethylphosphorous acid. The reaction proceeded very violently with strong heat evolution, and even with boiling of the reaction mixture; during the process of reaction, considerable increase in viscosity was observed. After standing for 24 hours at room temperature the reaction mixture was fractionally distilled in vacuo from a small Arbuzov flask. From the fractional distillation there resulted a small quantity of initial dimethylphosphorous acid and 7.2 g of 1-dimethylphosphon-2-diethylphosphonethane;

b.p. 158-160° (2 mm); n_D^{20} 1.4430; d_4^{20} 1.2075; MR_D 60.82; calculated 60.87.

0.1460 g substance: 67.7 ml NaOH (T = 0.017841). Found %: P 23.1. $C_8H_{20}O_6P_2$. Calculated %: P 23.4.

Addition of Diethylphosphorous Acid to Vinylphosphinic Ester. A saturated solution of sodium ethylate in ethyl alcohol was added dropwise to the reaction mixture which consisted of 6 g of vinylphosphinic ester and 5 g of diethylphosphorous acid. The reaction proceeded as vigorously as in the preceding experiment. From fractional distillation of the reaction mixture, there resulted 6.3 g of 1,2-di(diethylphosphone)ethane;

b.p. 164-165° (2 mm); n_D^{20} 1.4410; d_4^{20} 1.1376; MR_D 70.13; calculated 70.10.

0.1614, 0.1526 g substance: 6.6, 6.35 ml NaOH (T = 0.017841). Found %: P 20.2, 20.5. $C_{10}H_{24}O_6P_2$. Calculated %: P 20.5

Addition of Dibutylphosphorous Acid to Vinylphosphinic Ester. Reaction was carried out with 4.6 g of vinylphosphinic ester and 5.5 g of dibutylphosphorous acid in the presence of sodium butylate. From the first fractional distillation of the reaction mixture, 5.2 g of 1-diethylphosphon-2-dibutylphosphonethane resulted;

b.p. 197-199° (2 mm); n_D^{20} 1.4430; d_4^{20} 1.0681; MR_D 88.6; calculated 88.1

0.1435 g substance: 49.8 ml NaOH (T = 0.017841). Found %: P 17.1. $C_{14}H_{32}O_6P_2$. Calculated %: P 17.3

Addition of Ammonia to Vinylphosphinic Ester. Experiment I. 10.4 g of the vinylphosphinic ester was added to 65 g of concentrated aqueous ammonia. The mixture was left standing at room temperature for 24 hours. After distilling off the ammonia and water in low vacuum, the residue was a hard glassy mass.

Experiment II. 7 g of vinylphosphinic ester was added to 54.5 g of ethyl alcohol containing 10 g of ammonia. After standing for 24 hours at room temperature in a covered flask, followed by subsequent fractional distillation, the initial products were recovered (with the exception of a small fraction boiling in the range of 95-100° at 5 mm).

Experiment III. The experiment was carried out identically with the preceding, using 15 g of vinylphosphinic ester in the presence of sodium methylate. There resulted, upon fractional distillation of the reaction mixture, 11 g of the ethyl ester of β-diethylphosphonethylamine;

b.p. 93-95° (4 mm); n_D^{20} 1.4270; d_4^{20} 1.0515; MR_D 44.20; calculated 44.19.

0.1486 g substance: 47.4 ml NaOH (T = 0.017841). Found %: P 16.6. $C_6H_{16}O_3NP$. Calculated %: P 17.0.

Addition of Dimethylamine to Vinylphosphinic Ester. 4.5 g of dimethylamine was added to 5 g of vinylphosphinic ester. Heat evolution from the reaction mixture was observed up to 55°. The mixture was left standing at room temperature for 24 hours, after which it was fractionally distilled in vacuo. 5.3 g of β-diethylphosphonethyldimethylamine resulted;

b.p. 103-104° (4 mm); n_D^{20} 1.4345; d_4^{20} 1.0157; MR_D 53.6; calculated 53.9.

0.1455 g substance: 44.2 ml NaOH (T = 0.017841). Found %: P 14.9. $C_8H_{20}O_3NP$. Calculated %: P 14.8.

Action of Dimethylamine Upon Ethyl β-Bromethylphosphinic ester. A mixture of 10 g of β-bromethylphosphinic ester, 7.5 g of dimethylamine and 25 ml of water was left standing for 2 hours. 25 ml of 20% caustic soda solution was then added to it. The reaction mixture was then extracted with 100 ml of benzene, the benzene solution dried with calcium chloride, the benzene distilled off on a water bath, and the residue distilled in vacuo. 3.2 g of β-diethylphosphonethyldimethylamine resulted;

b.p. 108-109° (6 mm); n_D^{20} 1.4340; d_4^{20} 1.0154.

Addition of Piperidine to Vinylphosphinic Ester. 3.7 g of piperidine was added to 5 g of vinylphosphinic ester. Little heat evolution from the reaction mixture was observed. It was left standing at room temperature for 24 hours and was then fractionated. 4 g of β-diethylphosphonethylpiperidine was separated:

b.p. 135-137° (3 mm); d_4^{20} 1.0514; n_D^{20} 1.4605; MR_D 64.82; calculated 65.5.

0.128 g substance: 32.9 ml NaOH (T = 0.017841). Found %: P 12.6. $C_{11}H_{24}O_3NP$. Calculated %: P 12.5.

An analogous product resulted from β-bromethylphosphinate and piperidine.

Addition of Aniline to Vinylphosphinic Ester. Sodium methylate solution was added dropwise to a mixture of 7 g of vinylphosphinic ester and 4 g of aniline. Temperature of the reaction mixture rose rapidly to 70°. After the temperature fe ll, the reaction mixture was then heated on a water bath for 1 hour, and then left to stand for 48 hours at room temperature. Upon fractional distillation of the reaction mixture, there was separated 1.5 g of fraction with b.p. 145-150° (6 mm), along with a considerable quantity of lower boiling fractions:

b.p. 145-150° (6 mm); n_D^{20} 1.4910; d_4^{20} 1.0947; MR_D 68.03; calculated 68.36.

0.1445 g substance: 33.3 ml NaOH (T = 0.017841). Found %: P 11.5. $C_{12}H_{18}O_3NP$. Calculated %: P 12.0.

SUMMARY

1. A new type of reaction — phosphonethylation — has been discovered, consisting of the addition of various nucleophilic reagents to the ethyl ester of vinylphosphinic acid.

2. By the addition of dialkylphosphorous acids, ammonia and amines to vinylphosphinic ester, there have been obtained, respectively, 1,2-di-(dialkylphosphon)-ethanes and β-diethylphosphonethylamine and its homologs.

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[3] A Ford-Moore and J. Williams, J. Chem. Soc., 1465 (1947).

[4] J. Finkelstein, J. Am. Chem. Soc., 68, 2397 (1946).

[5] G. Kosollapoff, J. Am. Chem. Soc., 69, 2112 (1947).

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• See Consultants Bureau English translation, page 423.
•• See Consultants Bureau English translation, page 531.

THE SYNTHESIS AND PROPERTIES OF VINYLPHOSPHINIC ESTERS

II. THE PHOSPHONETHYLATION REACTION, ADDITION OF MALONIC, CYANACETIC AND ACETOACETIC ESTERS AND THEIR HOMOLOGS TO VINYLPHOSPHINIC ESTER

A. N. Pudovik and O. N. Grishina

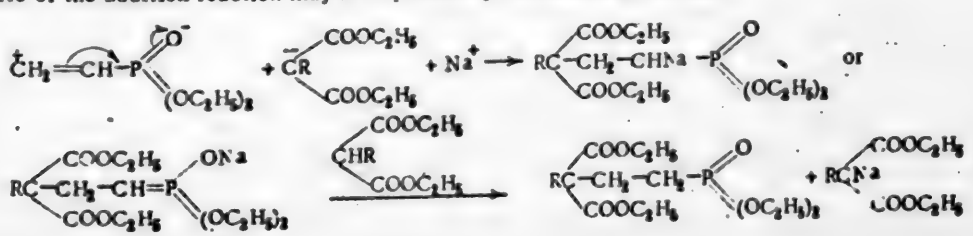
In their previous article, the authors described addition reactions of dialkylphosphorous acids, ammonia and certain secondary amines to vinylphosphinic ester. It was demonstrated that these reaction proceed very smoothly in the presence of catalysts – alcoholates of the alkali metals, and in some cases also without, by simply mixing the two substances together. As a result there were obtained a number of di-(diphosphon)-ethane esters, the ethyl ester of β-aminoethylphosphinic acid and a number of its derivatives. In view of the considerable theoretical and practical implications of the phosphonethylation reaction which has been discovered by the authors, they have proceeded to extend the investigations carried out so far, and in the present work have studied the addition reactions of malonic, cyanacetic and acetoacetic esters and their homologs, and benzyl cyanide, to vinylphosphinic ester. All of the compounds enumerated possess mobile hydrogen atoms in a methylene group, and their addition to various types of α-β-unsaturated electrophilic reagents – such as unsaturated acids and their derivatives, aldehydes, ketones, nitriles, nitrocompounds, and others – has been the object of numerous investigations for many decades. A study of the addition of malonic, cyanacetic and acetoacetic esters to unsaturated organophosphorous compounds has not been carried out up to the present time.

As in the preceding work, the authors have used the ethyl ester of vinylphosphinic acid as an unsaturated electrophilic reagent, which has been found to be the simplest and most accessible of the vinylphosphinic esters known up to the present time. All reactions have been carried out in the presence of small quantities of alkali metal alcoholates: without the use of catalysts, the reaction fails to go. It was noted that the purest products, boiling within a narrow temperature range, were obtained when sodium ethylate was used as the catalyst. When using the alcoholates of other alcohols, there is an exchange of radicals between the alcohol and the ester groups of the reactants, which ultimately leads to formation of side products and to contamination, by the same token, of the main reaction product. All of the reactions proceeded with considerable heat evolution from the reaction mixture, which, in some cases, attained 80-100°, especially upon rapid addition of the ethylate solution, and was accompanied by a violent boiling up of the reaction mixture. As preliminary experiments have demonstrated, there is no resinification of the vinylphosphinic ester; neither was there observed a decrease in the yields of addition products as compared with experiments carried out at low temperatures. Therefore, the reaction was allowed to continue further without special cooling of the reaction mixtures, but with slow gradual addition of sodium methylate. The procedural method adopted allows the reactions to be carried out easily and in a very short time.

Only one product resulted from the reaction between equimolecular quantities of malonic and of vinylphosphinic esters – the ethyl ester of β-diethylphosphonethylmalonic acid in 80% yield: under these conditions, the addition product of malonic ester to two molecules of vinylphosphinic ester was not found.

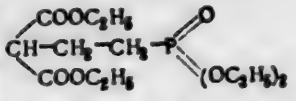
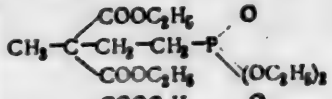
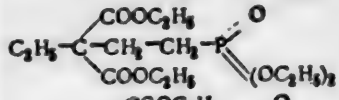
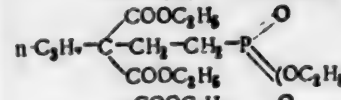
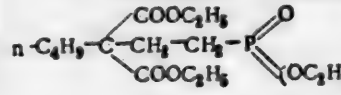
The addition of the malonic ester homologs – methyl-, ethyl-, propyl- and n-butyl-malonic esters – to vinylphosphinic ester, in the presence of sodium ethylate, proceeds very smoothly: the corresponding ethyl esters of β-diethylphosphonethylalkylmalonic acid result in good yield. Values for the molecular refraction constants, and yields of addition products, are presented in Table 1.

The course of the addition reaction may be expressed by the following scheme:



where: R = H, CH_3, C_2H_5, n-C_3H_7, n-C_4H_9

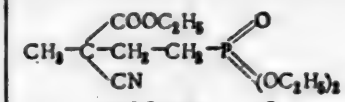
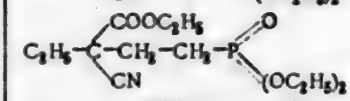
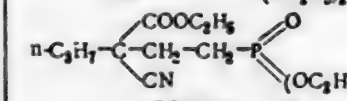
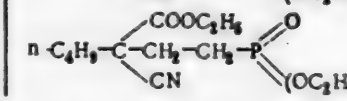
TABLE 1

No.	Formula	Boiling point	d_4^{20}	n_D^{20}	MR_D Found	MR_D Calculated	Yield (in %)
1		158-159° (1 mm)	1.1316	1.4420	76.41	75.83	79.6
2		175-177° (4 mm)	1.1021	1.4400	81.0	80.98	78.9
3		162° (2.5 mm)	1.0925	1.4423	85.64	85.39	59.2
4		175-176° (2 mm)	1.0782	1.4425	90.26	90.00	78.4
5		185-186° (2.5 mm)	1.0640	1.4432	94.88	94.82	86.41

Diethylphosphonethylamalonic ester and its homologs are viscous, colorless liquids with a faint pleasant odor, insoluble in water, readily soluble in alcohol and in ether.

Two addition products — β-diethylphosphonethylcyanacetic ester, and di-(β diethylphosphonethyl)-cyanacetic ester, resulted from reaction with cyanacetic ester upon combining equimolecular quantities of the reactants. The total yield of products was 62%. Fractional distillation of the reaction mixture was accompanied by

TABLE 2

No.	Formula	Boiling point	d_4^{20}	n_D^{20}	MR_D Found	MR_D Calculated	Yield (in %)
1		165-166° (2 mm)	1.0989	1.4430	70.28	69.96	88.9
2		166-167° (3.5 mm)	1.0849	1.4440	74.76	74.57	66.2
3		173-174° (2 mm)	1.0702	1.4443	79.28	79.19	83.7
4		177-178° (3.5 mm)	1.0564	1.4460	84.16	83.81	77.7

considerable decomposition, even with the use of high vacuum, which was no doubt reflected in both the yields of products and their purity. In all of the experiments carried out, both products, and especially the di-(β-diethylphosphonethyl)-cyanacetic ester, were always yellow in color, and at times yellow-brown. Fractional distillation of the addition products of cyanacetic ester homologs with vinylphosphinic ester proceeded without visible signs of decomposition. The synthesized ethyl esters of β-diethylphosphonethylalkylcyanacetic acid were found to be quite viscous, colorless, or faintly colored to yellow liquids, insoluble in water.

Values for the molecular refraction constants, and the yields of obtained ethyl esters of β-diethylphosophenethylalkylcyanacetic acid are given in Table 2 above.

To prove the structure of the products obtained, one of them – the ethyl ester of β-diethylphosphonethylcyanacetic acid – was synthesized by the authors according to another method: by reacting the ethyl ester of β-bromethylphosphinic ester with the sodium derivative of ethylcyanacetic acid ester. The product obtained corresponded in its constants exactly to the ethyl ester of β-diethylphosphonethylethylcyanacetic acid as obtained by the method of the authors.

The addition of acetoacetic ester and of its homologs to vinylphosphinic ester proceeds with greater difficulty as compared with malonic and cyanacetic esters and their homologs. A considerable quantity of catalyst had to be added to the mixture, and prolonged heating applied, to promote reaction. However, even under these conditions, the yields of products remained very negligible, of the order of 15-20%; fractional distillation of the reaction mixtures was accompanied by quite considerable decomposition, with formation of considerable quantities of low-boiling products.

To conclude, the addition reaction of benzyl cyanide to vinylphosphinic ester was carried out. The reaction proceeded very vigorously, with formation chiefly of di-(β-diethylphosphonethyl)-benzyl cyanide, and only very small quantities of β-diethylphosphonethylbenzylcyanide. Total yields of both addition products consituted about 20%.

The addition of cyanacetic and acetoacetic esters, their homologs, and of benzyl cyanide to vinylphosphinic ester can be expressed by schemes similar to the one given above for the reaction with malonic ester.

EXPERIMENTAL

Addition of Malonic Ester to Vinylphosphinic Ester. A saturated solution of sodium ethylate in ethyl alcohol was added dropwise to the reaction mixture which consisted of 8.5 g of vinylphosphinic ester and 10 g of malonic ester. A strong heat evolution from the reaction mixture was observed. Following addition of the requisite quantity of ethylate necessary to complete the reaction (to the cessation of heat evolution) which proceeded for 10-15 minutes, with one hour standing at room temperature, the mixture was redistilled in vacuo. 10.5 g of the diethyl ester of β-diethylphosphonethylmalonic acid resulted (Table 1:1).

0.1564, 0.1573 g substance: 31.62, 31.82 ml NaOH (T = 0.017841). Found %: P 9.99, 9.99. $C_{13}H_{25}O_7P$. Calculated %: P 9.55.

Addition of Malonic Ester Homologs to Vinyl Phosphinic Ester. Reaction was carried out according to a procedure similar to that carried out in the preceding experiment.

Addition of Methylmalonic Ester. The reaction was carried out between 4.9 g of vinylphosphinic ester and 5.2 g of the ethyl ester of methylmalonic acid. 6 g of the diethyl ester of β-diethylphosphonethylmethylmalonic acid resulted from two fractional distillations (Table 1:2).

0.1525 g substance: 29.2 ml NaOH (T = 0.017841). Found %: P 9.46. $C_{14}H_{27}O_7P$. Calculated %: P 9.14.

Addition of Ethylmalonic Ester. 6 g of vinylphosphinic and 10 g of ethylmalonic esters were taken for reaction. 3.5 g of ethylmalonic ester was recovered during fractional distillation of the reaction mixture. There resulted 7.2 g of the ethyl ester of β-diethylphosphonethylethylmalonic acid (Table 1:3).

0.1526, 0.1528 g substance: 26.43, 26.78 ml NaOH (T = 0.017841). Found %: P 8.56, 8.66. $C_{15}H_{29}O_7P$. Calculated %: P 8.79.

Addition of Propylmalonic Ester. Reaction was carried out with 7.02 g of the ethyl ester of propylmalonic acid and 5.7 g of vinylphosphinic ester. 7.8 g of the ethyl ester of β-diethylphosphonethylpropylmalonic acid resulted (Table 1:4).

0.1508, 0.1506 g substance: 26.6, 26.5 ml NaOH (T = 0.017841). Found %: P 8.71, 8.66. $C_{16}H_{31}O_7P$. Calculated %: P 8.46.

Addition of Butylmalonic Ester. Reaction was carried out with 5.7g of vinylphosphinic ester and 7.6 g of the ethyl ester of butylmalonic acid. 7.8 g of the ethyl ester of β-diethylphosphonethylbutylmalonic acid resulted (Table 1:5).

0.1517, 0.1524 g substance: 25.55, 25.62 ml NaOH (T = 0.017841). Found %: P 8.32, 8.30. $C_{17}H_{33}O_7P$. Calculated %: P 8.14.

Addition of Cyanacetic Ester to Vinylphosphinic Ester. 8.2 g of cyanacetic ester was added to 12 g of vinylphosphinic ester, after which a saturated solution of sodium ethylate was slowly added dropwise to the reaction mixture. Reaction proceeded very vigorously, the addition of each drop being accompanied by evolution of heat from the reaction mixture. Dropwise addition was continued for 15-20 minutes, with periodic cooling of the reaction mixture with water. Partial decomposition of the reaction mass was observed during the distillation process; condenser and receiving flasks during the distillation were filled at all times with white vapors. As the result of the first fractional distillation, three fractions were separated: 1) 65-170° (4 mm) – 2 g; 2) 170-177° (4 mm) – 4.1 g; 3) 206-255° (8 mm) – 8.8 g. As the result of repeated distillation of these three fractions, 3.1 g of the ethyl ester of β-diethylphosphonethylcyanacetic acid with b.p. 166-167° (2 mm) was obtained: n_D^{20} 1.4430; d_4^{20} 1.0740.

0.1555 g substance: 35.73 ml NaOH (T = 0.017841). Found %: P 11.35. $C_{11}H_{20}O_5NP$. Calculated %: P 11.17.

At the same time, there resulted 5.8 g of the ethyl ester of di-(β-diethylphosphonethyl)-cyanacetic acid, with b.p. 227° (2 mm): n_D^{20} 1.4540; d_4^{20} 1.3830.

0.1535, 0.1585 g substance: 45.4, 45.74 ml NaOH (T = 0.017841). Found %: P 14.61, 14.26. $C_{17}H_{33}O_8NP_2$. Calculated %: P 14.07.

Addition of Cyanacetic Ester Homologs to Vinylphosphinic Ester. Addition of Methylcyanacetic Ester. 4.8 g of the ethyl ester of methylcyanacetic acid and 6.2 g of vinylphosphinic ester were taken for reaction. Decomposition was not observed during fractional distillation of the reaction products. 5.25 g of the ethyl ester of β-diethylphosphonethylmethylcyanacetic acid resulted (Table 2:1).

0.1528, 0.1537 g substance: 31.61, 32.18 ml NaOH (T = 0.017841). Found %: P 10.22, 10.34. $C_{12}H_{22}O_5NP$. Calculated %: P 10.63.

Addition of Ethylcyanacetic Ester. Reaction was carried out with 7 g of ethylcyanacetic ester and 6 g of vinylphosphinic acid. 5.4 g of the ethyl ester of β-diethylphosphonethylethylcyanacetic acid resulted (Table 2:2

0.1512, 0.1504 g substance: 31.36, 30.80 ml NaOH (T = 0.017841). Found %: P 10.24, 10.18. $C_{13}H_{24}O_5PN$. Calculated %: P 10.15.

Addition of Propylcyanacetic Ester. 5.6 g of propylcyanacetic ester and 5.9 g of vinylphosphinic ester were taken for reaction. As the result of repeated distillation of the reaction mixture, 4.98 g of the ethyl ester of β-diethylphosphonethylpropylcyanacetic acid was obtained (Table 2:3).

0.1521 g, 0.1490 g substance: 30.00, 29.22 ml NaOH (T = 0.017841). Found %: P 9.74, 9.69. $C_{14}H_{26}O_5PN$. Calculated %: P 9.70.

Addition of Butylcyanacetic Ester. The reaction was carried out with 6 g of vinylphosphinic ester and 5.8 g of butylcyanacetic ester. 7.95 g of the ethyl ester of β-diethylphosphonethylbutylcyanacetic acid resulted (Table 2:4).

0.1508, 0.1504 g substance: 28.54, 28.68 ml NaOH (T = 0.017841). Found %: P 9.35, 9.42. $C_{15}H_{28}O_5PN$. Calculated %: P 9.29.

Action of Sodiumethylcyanacetic Ester upon the Ethyl Ester of β-Bromethylphosphinic Acid. 5.7 g of ethylcyanacetic ester was added to an alcoholic solution of sodium ethylate prepared from 0.93 g of sodium and 14 ml of ethyl alcohol, and 10 g of the ethyl ester of β-bromethylphosphinic acid was then added dropwise. Strong heat evolution from the reaction mixture was observed. After all of the ethyl ester of β-bromethylphosphinic acid had been added, the reaction mixture was heated for 2 hours on a water bath. The precipitate of sodium bromide was filtered off, the alcohol distilled off, and the residue was redistilled in vacuo. 5.9 g of the ethyl ester of β-diethylphosphonethylethylcyanacetic ester resulted, with b.p. 167° (4 mm): n_D^{20} 1.4440; d_4^{20} 1.0852.

Addition of Acetoacetic Ester to Vinylphosphinic Ester. A saturated solution of sodium ethylate in ethyl alcohol was added dropwise to a reaction mixture consisting of 8.9g of vinylphosphinic ester and 6.4 g of acetoacetic ester. Reaction began only after the addition of a considerable volume of alcoholic solution (1-2 ml), and there was not observed any strong evolution of heat. After 1 hour of heating on a water bath, the reaction mixture was fractionally distilled in vacuo. Fractional distillation was accompanied by considerable decomposition of the reaction mixture. After repeated fractional distillation, 2.23 g of ethyl ester of

β-diethylphosphonethylacetoacetic acid with b.p. 170-172° (4 mm) resulted: n_D^{20} 1.4510.

0.1512 g substance: 30.72 ml NaOH (T = 0.017841). Found %: P 10.03. $C_{12}H_{23}O_6P$. Calculated %: P 10.53.

Addition of Propylacetoacetic Ester to Vinylphosphinic Ester. Reaction was carried out between 8.9 g of vinylphosphinic ester and 9.1g of propylacetoacetic ester. After repeated fractional distillation of the reaction mixture, 3.1 g of the ethyl ester of β-diethylphosphonethylpropylacetoacetic acid, with b.p. 138-141° (2 mm) resulted: n_D^{20} 1.4430.

0.1510, 0.1504 g substance: 30.35, 29.47 ml NaOH (T = 0.017841). Found %: P 9.93, 9.68. $C_{13}H_{27}C_6P$. Calculated %: P 9.61.

Addition of Benzyl Cyanide to Vinylphosphinic Ester. A saturated solution of sodium ethylate was added dropwise to a reaction mixture composed of 6.8 g of vinylphosphinic ester and 4.9 g of benzyl cyanide. Reaction proceeded very vigorously. The reaction mixture which was colorless at the start of the reaction became lilac in color by the end of the reaction, and also became very viscous. After a triple fractionation, accompanied by a small amount of decomposition, 1.5 g of di-(β-diethylphosphonethyl)-benzylcyanide, with b.p. 247-248° (2 mm) resulted: n_D^{20} 1.4940.

0.1510, 0.1514 g substance: 41.10, 41.24 ml NaOH (T = 0.017841). Found %: P 13.45, 13.46. $C_{20}H_{33}O_6NP_2$. Calculated %: P 13.01.

SUMMARY

It has been demonstrated that malonic, cyancetic and acetoacetic esters, and their homologs, as well as benzyl cyanide, add easily in the presence of sodium ethylate to the ethyl ester of vinylphosphinic acid, with the formation, respectively, of diethylphosphonethyl-malonic, cyanacetic and acetoacetic esters, and their homologs, and di-(β-diethylphosphonethyl)-benzylcyanide.

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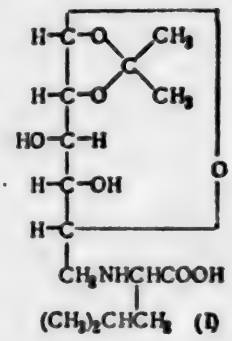
CARBOHYDRATE DERIVATIVES OF AMINO ACIDS

II. CONDENSATION OF MONOACETONEANHYDROGLUCOSE WITH LEUCINE AND GLUTAMIC ACID

V. I. Kovalenko

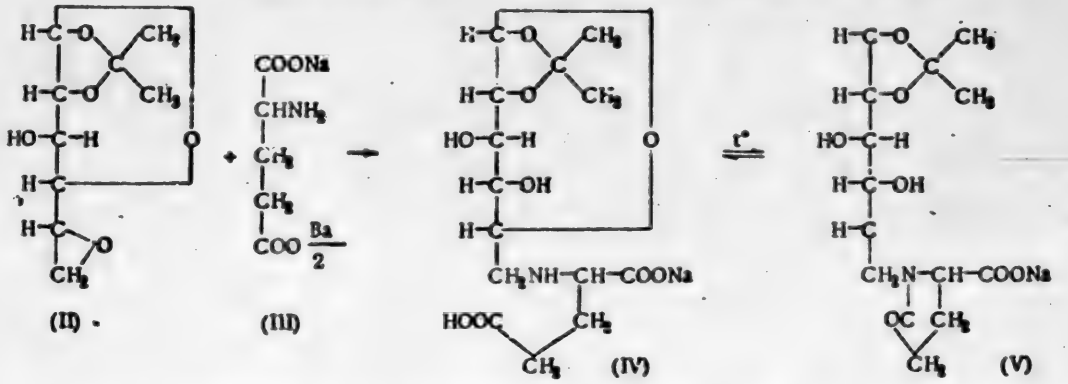
As was shown in the preceding article* on the synthesis of carbohydrate-amino acid compounds, the author developed a method for condensing barium salts of amino acids with anhydroglucose. Utilizing this method, the author has condensed monoacetoneanhydroglucose with d,l-leucine, and has obtained 1,2-monoacetonequinovosyl-6-d,l-leucine (I), which precipitates in crystalline form from a hot solution after removal of the barium.



(I)

It was of interest to synthesize a carbohydrate derivative of glutamic acid which is involved in the formation of glutathione, and which plays an essential role in the construction of plant proteins. Some investigators (Abderhalden [1]) have expressed an opinion that glutamic acid bears a direct relationship to the synthesis of pyrrole compounds – both the simple [2] and the more complex [3].

By condensing anhydroglucose (II) with l-glutamic acid, taken in the form of its double sodium and barium salt (III), the author has obtained the sodium salt of 1,2-monoacetonequinovosyl-6-N-α-pyrrolidone-α'-carboxylic acid (V), instead of the sodium salt of 1,2-monoacetonequinovosyl-6-N-l-glutamic acid (IV).



(II) (III) (IV) (V)

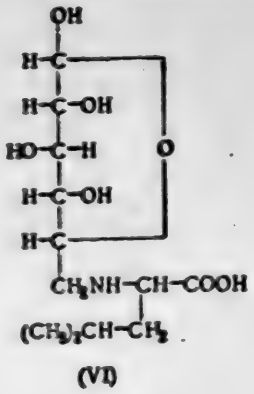
This is conditioned by the fact that glutamic acid and its derivatives readily form the lactam, or an internal anhydride, frequently called α-pyrrolidone carboxylic acid [4]. V. Skola [5] established that in 2% aqueous solution, the ratio of glutamic to pyrrolidonecarboxylic acid is equal to 1:52. The high temperature and concentration of the solution displace the equilibrium to the side of the cyclic state.

Therefore, it can be considered that in the author's case, an equilibrium occurs between forms (IV) and (V), although considering the fact that isolation of substance (IV) is connected with evaporation of the solution at a temperature of 50-95°, it should be assumed that the main bulk is in the form of the sodium salt of 1,2-monoacetonequinovosyl-6-N-α-pyrrolidonecarboxylic acid.

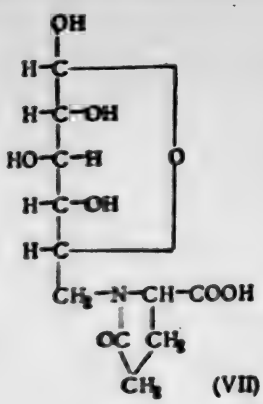
After cleavage of the acetone radical from substances (I) and (V), quinovosyl-6-N-l-leucine (VI) and quinovosyl-6-N-α-pyrrolidone-α'-carboxylic acid (VII) resulted. (See diagram on next page).

Upon hydrolysis, compound (VII), which is affected by acetic acid converts into (VIII), and this is related to the appearance of a mobile hydrogen atom at the nitrogen atom, with increased ability to produce colored products in acid solution when in contact with oxygen of the air. This is in conformity with the data given in the article, and also with the observation of M. Wolfrom [6]. Substances (VI) and (VII) do not mutarotate in aqueous solution.

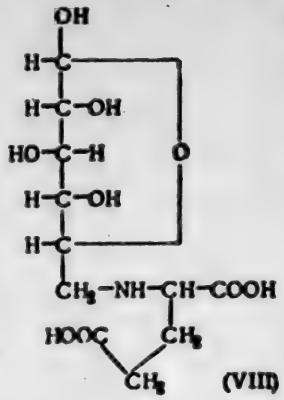
* J. Gen. Chem. 23, 86 (1953). (Consultants Bureau translation, p.83).



(VI)



(VII)



(VIII)

EXPERIMENTAL

1. Reaction of Anhydroglucose with Leucine.

a) Synthesis of 1,2-Monoacetonequinovosyl-6-N-d, l-leucine (I). 1.8 g (13.7 millimoles) of racemic leucine was dissolved by heating in 83.5 ml of 0.2 N barium hydroxide. 2.3 g (11.3 millimoles) of anhydroglucose was added. The rest of the procedure was as in the case of glycine (see Article I). After heating for 2 hours, the barium was precipitated with 35.7 ml of 0.4 N sulfuric acid and the hot solution was filtered through a funnel constructed for hot filtering. The sediment on the filter was washed twice with hot water (using 20-25 ml portions) and the wash waters collected separately. After cooling, white, needle crystals separated; filtered, washed with absolute alcohol and ether, and the filtrate tested for complete barium precipitation, and if absent, vaporized in vacuo together with the wash waters, to a volume of 20-25 ml. After cooling, large crystals separated out again, which were separated, washed with alcohol and ether, and then dried in vacuo and combined with the main bulk of crystals. The yield was 2.45 g (51.8% of theoretical). The substance melted at 216-220° (with decomposition).

$[\alpha]_D^{24}$ −12.6° (c = 1.011; water). 0.1230 g substance: 3.67 ml 0.1 N H_2SO_4. 0.1438 g substance: 4.09 ml 0.1 N H_2SO_4. Found %: N 4.18, 3.98. $C_{15}H_{27}O_7N$. Calculated %: N 4.20.

The synthesized product was readily soluble in water and acetic acid, and with heating somewhat soluble in dilute alcohol (methyl, ethyl), insoluble in acetone, ether, gasoline. The aqueous solution gave an acid reaction to litmus and upon heating dissolved barium carbonate.

In a similar fashion, as with racemic leucine, condensation of anhydroglucose with l-leucine was carried out, at which time monoacetonequinovosyl-6-N-l-leucine resulted.

b) Hydrolysis of 1,2-Monoacetonequinovosyl-6-N-l-leucine (VI). 2.12 g of the condensation product between anhydroglucose and l-leucine was heated in a hydrogen atmosphere for 3.5 hours with 55 ml of 50% acetic acid, proceeding then as in the case of glycine. The residue in the flask was dissolved by heating in 50 ml of absolute ethanol, from which light-brown crystals precipitated out upon cooling. Filtered and washed with absolute isopropyl alcohol. Yield was 0.28 g (15.6% of theoretical). The substance melted at 208-210° (with decomposition). After decolorization of the filtrate with carbon, followed by evaporation at room temperature in an open beaker to a volume of 5-6 ml, there resulted another 0.5 g of the product. Quinovosyl-6-N-l-leucine is soluble in water, dilute methyl and ethyl alcohols, insoluble in absolute isopropyl alcohol, acetone, chloroform and pyridine.

$[\alpha]_D^{23}$ + 33.7° (c = 0.861; water).

0.1322 g substance: 4.36 ml 0.1 N H_2SO_4. 0.0966 g substance: 3.14 ml 0.1 N H_2SO_4. Found %: N 4.62, 4.59. $C_{12}H_{23}O_7N$. Calculated %: N 4.77%.

2. Reaction between Anhydroglucose and Glutamic Acid.

a) Synthesis of the Sodium Salt of 1,2-Monoacetonequinovosyl-6-N-α-pyrrolidone-α"-carboxylic acid (V). The double barium and sodium salt of glutamic acid was prepared by dissolving 1.1 g (6.5 millimoles) of sodium glutamate in 30 ml of 0.2 N-barium hydroxide. 1.2 g (6 millimoles) of anhydroglucose was added to the resulting solution. The solution was heated under reflux for one hour, an equivalent quantity

of sulfuric acid (16.3 ml of 0.4 N) was added to the hot solution, filtered, and tested for complete precipitation of barium. The filtrate was evaporated in vacuo at a bath temperature of 50-60°, and the residue in the flask then dried for several minutes at 95-100°. The contents of the flask were then dissolved in 12 ml of methanol with heat, and the reaction product precipitated with 6 ml of dry acetone. The precipitate was filtered rapidly and washed with dry acetone. It was obtained in the form of a white, very hygroscopic powder, readily soluble in water, aqueous alcohol, insoluble in acetone, ether, benzene, chloroform. Yield 1.14 g, or 45.8% of theoretical.

$[\alpha]_D^{24} -6.5°$ (c = 3.43; water).

After prolonged drying in a desiccator, the substance melted at 160-163°.

0.1696 g substance: 4.88 ml 0.1 N H_2SO_4. 0.1594 g substance: 4.60 ml 0.1 N H_2SO_4. 0.1210 g substance: 0.239 g Na_2SO_4. 0.1346 g substance: 0.268 g Na_2SO_4. Found %: N 4.02, 4.04. Na 6.40, 6.43. $C_{14}H_{20}O_8NNa$. Calculated %: N 3.96; Na 6.51.

b) Hydrolysis of Sodium 1,2-Monoacetonequinovosyl-6-N-α-pyrrolidone-α'-carboxylate. 1.46 g of sodium 1,2-monoacetonequinovosyl-6-N-α-pyrrolidone-α'-carboxylate dissolved in 25 ml of 50% acetic acid was heated 3.5 hrs. in a hydrogen atmosphere. The procedure was further carried out as described in article I. The residue in the flask, which consisted of the amorphous substance and sodium acetate, was ground well with 5 ml of dry acetone and 5 ml of absolute methanol, filtered, the filtrate evaporated in vacuo, and then dissolved with gentle heating in 4 ml of absolute methanol, and filtered again if necessary, and the solution mixed with 10 ml of absolute ether. The solution was poured off from the resulting viscous oil and the oil dried over sulfuric acid in a vacuum desiccator. A very hygroscopic powder results, readily soluble in water and alcohols and insoluble in other solvents. The aqueous solution of quinovosyl-6-N-α-pyrrolidonecarboxylic acid possessed an acid reaction toward litmus. The product melted at 120-130° and did not give a color with aqueous ninhydrin solution. Yield was 0.8 g (66% of theoretical).

$[\alpha]_D^{26} +26.5°$ (c = 1.284; water).

0.1368 g substance: 4.58 ml 0.1 N H_2SO_4. 0.1242 g substance: 4.10 ml 0.1 N H_2SO_4. Found %: N 4.68, 4.62. $C_{11}H_{17}O_8N$. Calculated %: N 4.82.

SUMMARY

As the result of condensation between anhydroglucose and leucine and with glutamic acid, the following have been obtained: monoacetonequinovosyl-6-l-leucine and the sodium salt of monoacetonequinovosyl-6-N-α-pyrrolidone-α''-carboxylic acid, and after cleavage of acetone there has been separated: quinovosyl-6-N-l-leucine and quinovosyl-6-N-α-pyrrolidone-α'-carboxylic acid, which represents carbohydrate derivatives of amino acids with a free reducing group capable of entering into various chemical reactions.

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CARBOHYDRATE DERIVATIVES OF AMINO ACIDS

III. CONDENSATION OF ANHYDROGLUCOSE WITH TYROSINE

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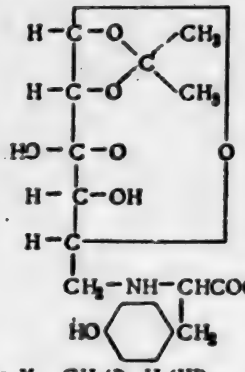
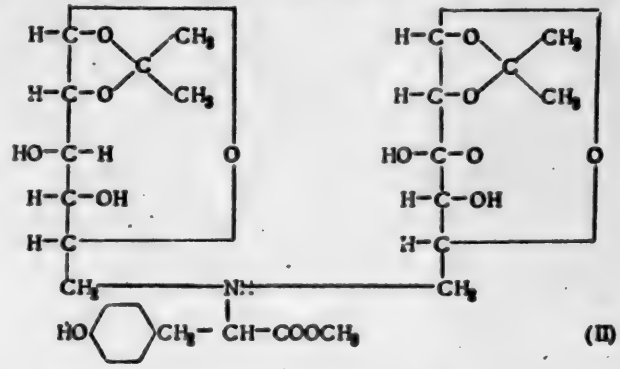
In the preceding articles the authors have described a synthesis for aliphatic quinovosylamino acids, derived from glycine, leucine and glutamic acid. It will be shown in the present work that when anhydroglucose is condensed with the methyl ester of tyrosine, there result the methyl esters of monoacetonequinovosyl-6-N-l-tyrosine (I) and bis-(monoacetonequinovosyl-6-6')-N-l-tyrosine (II). Condensation with the barium salt of tyrosine also proceeds readily: from the barium salt of monoacetonequinovosyl-6-N-l-tyrosine a free acid (III) was separated:





(II)

where X = CH_3(I); H (III).

Three functional groups are contained in the tyrosine molecule (COOH, OH, NH_2), which are able to add to the ethylene oxide ring of anhydroglucose. The separation of the barium salt of monoacetonequinovosyl-6-N-tyrosine as the principal reaction product indicated that the carboxyl group does not participate in this reaction.

In the case of phenolic hydroxyl addition to the ethylene oxide ring of anhydroglucose, a phenol ester should have resulted. However, compounds (I), (II) and (III) gave the Millon reaction, indicating the presence of free phenolic hyd-oxyl in tyrosine [1].

Theratio of quinovosyl derivatives of tyrosine and its methyl ester to diazobenzenesulfoacid may serve as indirect confirmation of the fact that compounds (I), (II) and (III), as obtained by the authors, possess the structures which have been ascribed to them. It is known that tyrosine and its esters will couple with diazobenzenesulfoacid [2] to form a red dye. If, however, tyrosine is benzoylated, then its ability to couple disappears [3]. The authors have observed a red coloration upon combining diazobenzenesulfoacid in soda solution with the quinovosyl derivative of tyrosine and its methyl ester, but after treating substances (I), (II) and (III) with benzoyl chloride, they no longer enter into azo linkage reaction. It is obvious that if condensation between anhydroglucose and tyrosine (and its ester) were to be accomplished at the expense of the phenolic hydroxyl, then conjugation with diazobenzenesulfoacid should have occurred after benzoylation also, since alkylated phenols enter into azo conjugation on reactions.

As the result of cleavage of the acetone group from compound (III), quinovosyl-6-N-l-tyrosine resulted, readily soluble in water, differing from the initial tyrosine wich is difficultly-soluble in water.

EXPERIMENTAL

a) Synthesis of 1,2-monoacetonequinovosyl-6-N-l-tyrosine(III): 56 ml of 0.2 N barium hydroxide was added to a suspension of 2.18 g (12 millimoles) of tyrosine in 300 ml of water and heated to complete solution of tyrosine. 2.24 g (11 millimoles) of anhydroglucose was added to the resulting solution and heated on a boiling water bath with reflux for 2 hours. The remainder of the procedure was as described in the general methods [4]. After evaporating the filtrate, the residue was boiled with 10 ml of water, filtered, washed with cold water, methyl and ethyl alcohols,

After drying 3 hours at 50-60°, the substance melted at 233-234° (with decomp.) The yield was 3 g (70.7% of theoretical). The reaction product – 1,2-monoacetonequinovosyl-6-N-l-tyrosine, was poorly soluble in water (1 part in 400 parts of water), ethyl, methyl alcohols and other organic solvents, more readily soluble in formic and acetic acids, and readily soluble in alkali and in mineral acids.

$[\alpha]_D^{21}$ – 27.7° (c = 0.267; water).

0.1418 g substance: 3.54 ml 0.1 N H_2SO_4. 0.1029 g substance: 2.61 ml 0.1 N H_2SO_4. Found %: N 3.50, 3.55. $C_{19}H_{25}O_8N$. Calculated %: N 3.65

The substance gave positive diazo reaction and also Millon reaction, and reduced Fehling's solution only after acid hydrolysis. The aqueous solution gave an acid reaction with litmus.

b) Hydrolysis of 1,2-monoacetonequinovosyl-6-N-l-tyrosine (III). 2 g of product (III) was dissolved, with heating, in 120 ml of 50% acetic acid and the hydrolysis was carried out for 3 hours according to the general procedure. After evaporation of the solvent and removal of the acetic acid, the residue in the flask was then boiled with 15 ml of acetone, ethyl acetate, 10 ml of 96% alcohol, and then with 10 ml of methyl alcohol. Filtered, washed with alcohol, ether and dried in a vacuum-desiccator. The resulting quinovosyl-6-N-l-tyrosine was a fine crystalline powder, slightly yellow in color, soluble in water, acetic acid, pyridine. Easily reduced Fehling solution upon heating, and upon heating with aqueous ninhydrin solution gave a violet coloration. The Millon test was positive. M.p. 215-220° (with decomp.) Yield 1.2 g (67% of theoretical).

$[\alpha]_D^{21}$ + 40.1° (c = 0.366; acetic acid: water = 2:1).

0.1476 g substance: 4.23 ml 0.1 N H_2SO_4. 0.1089 g substance: 3.10 ml 0.1 N H_2SO_4. Found %: N 4.01: 3.98. $C_{25}H_{27}O_8N$. Calculated %: N 4.07.

c) Isolation of the barium salt of 1,2-monoacetonequinovosyl-6-N-l-tyrosine. Barium salts of the acetone derivatives of quinovosylamino acids are formed by condensation of the barium salts of amino acids with anhydroglucose and do not usually separate out. Their separation may be carried out in the following manner: 0.7 g of l-tyrosine solution in 100 ml of 0.1 N barium hydroxide and 0.75 g of anhydroglucose are heated on a water bath with reflux for 2 hours. A strong current of carbon dioxide is then passed through the solution for 10-15 minutes, the barium carbonate separated, the filtrate tested for completeness of barium precipitation by the carbon dioxide, then evaporated to dryness at 60-70° in vacuo. The barium salt remaining in the flask was boiled with 15 ml of water. Filtered and dried. Yield 1.09 g (62% of theoretical). The barium salt decomposes at 215-220° and gives a positive diazo reaction.

$[\alpha]_D^{21}$ + 39.7° (c = 0.159; water).

0.1323 g substance: 0.0343 g $BaSO_4$. 0.1556 g substance: 0.0403 g $BaSO_4$. Found %: Ba 15.25, 15.24. $C_{38}H_{48}O_{16}N_2Ba$. Calculated %: Ba 15.22.

d) Synthesis of the methyl ester of 1,2-monoacetonequinovosyl-6-N-l-tyrosine (I). A well-ground mixture of equimolecular quantities of anhydroglucose (2 g) and the methyl ester of tyrosine (1.95 g), obtained by the method of E. Fischer [5], was heated in a hard glass test tube on a glycerol bath at 110-115° for 10 minutes. 30 ml of water was gradually added to the melt, cooled to 90°, and well stirred with a rod. The homogeneous solution was left 24 hours at room temperature, and the solvent was evaporated on a water bath to a residual volume of 8-10 ml. After cooling, crystals separated, were filtered off, washed with cold water, alcohol, acetone, and dried in a desiccator. Yield 2.4 g (61% of theoretical). The melting point of the methyl ester of monoacetonequinovosyl-6-N-l-tyrosine was 232-234°. It was insoluble in acetone, benzene, ether, dichlorethane, nitrobenzene, pyridine, acetic acid and pyridine-water mixture; partially soluble in hot water, soluble in formic acid. Gave a positive Millon reaction.

$[\alpha]_D^{24}$ + 14.8° (c = 1.217; absolute formic acid).

0.1217 g substance: 3.03 ml 0.1 N H_2SO_4. 0.1400 g substance: 3.46 ml 0.1 N H_2SO_4. Found %: N 3.49,3.46. $C_{19}H_{27}O_8N$. Calculated %: N 3.52.

Upon fusing the methyl ester of tyrosine with anhydroglucose in the presence of pyridine, the reaction became accelerated so much that the resulting methyl ester of 1,2-monoacetonequinovosyl-6-N-l-tyrosine was markedly contaminated by resinification products of anhydroglucose, resulting from the sharp temperature rise of the melt because of the reaction heat evolved.

e) Synthesis of the methyl ester of bis-(monoacetonequinovosyl-6,6'-)-N-l-tyrosine (II). A well-ground mixture of 0.8 g of monoacetoneanhydroglucose and 0.39 g of the methyl ester of tyrosine was heated for 1-1.5

minutes at 100°. The mixture formed rapidly a yellow melt, which was dissolved in 15 ml of water and decolorized with carbon. The water was evaporated in vacuo at 50-60°, the residue boiled with 10 ml of dry benzene, and then with 15 ml of dichlorethane. After filtration, the product was dissolved in 8 ml of absolute ethanol and precipitated with 15 ml of dry ether. It was filtered, washed with ether, and dried in a vacuum-desiccator. The light yellow, very hygroscopic substance was soluble in water and especially in aqueous alcohols, insoluble in the usual dry organic solvents. It decomposed at 100-110°. Yield was 1 g (83% of theoretical).

$[\alpha]_D^{28}$ −5.2° (c = 1.922; water).

0.1856 g substance: 2.90 ml 0.1 N H_2SO_4. 0.2863 g substance: 4.35 ml 0.1 N H_2SO_4. Found %: N 2.19, 2.13. $C_{28}H_{41}O_{13}N$. Calculated %: N 2.33

The aqueous solution of synthesized methyl ester of bis-(monoacetonequinovosyl-6,6')-N-l-tyrosine acquired a red-brown coloration upon heating with a 1% aqueous solution of ninhydrin. The Millon and diazo reactions were positive.

All synthesized tyrosine derivatives in soda solution gave positive diazo reactions, which consisted in the appearance of a red color upon combining a soda solution of the tyrosine derivative with diazobenzenesulfoacid solution. However, if 0.01-0.02 g of any of the tyrosine derivatives obtained by the authors were mixed with 4-5 ml of saturated soda solution, 3-4 drops of benzoyl chloride added and allowed to stand for several hours until the odor of the latter disappeared, then such benzoylated products no longer gave reaction with diazobenzenesulfoacid.

SUMMARY

1. It has been demonstrated that when monoacetoneanydroglucose is condensed with the barium salt of tyrosine, addition of the amino acid to the ethylene oxide ring of anhydroglucose proceeds at the expense of the amino groups, and not at the expense of the carboxyl and hydroxy groups.

2. The ethyl ester of bis-(monoacetonequinovosyl-6,6')-N-l-tyrosine, monoacetone-l-quinovosyl-6-N-l-tyrosine, and also quinovosyl-6-N-l-tyrosine and its barium and acetone derivatives have been synthesized.

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* See Consultants Bureau English translation, page 83.

THIAZOLYL DERIVATIVES OF ETHYLENE- AND TRIMETHYLENE-DIAMINE. I.

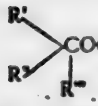
S. G. Fridman

At the present time the cause of a variety of allergic ailments is generally accepted as being due to histamine. Elucidation of the role of histamine has served to stimulate development of intensive research work in the field of synthesis of compounds possessing antihistaminic properties. Within the past few years a large number of such compounds have been synthesized. Fundamentally, these compounds may be divided into two groups, namely:

1) Ethylenediamine derivatives of the type:

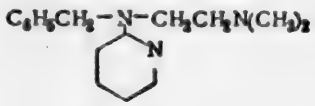
$NCH_2CH_2N(R''')_2$, where $R' = C_6H_5$, $C_6H_5CH_2$; $R'' = C_6H_5$ or the hetero-cyclic radical (pyridyl, pyramidyl, furfuryl, imidazolyl and others); $R''' = CH_3$ or $N(R'''')_2$ = the pyridine radical, pyrimidine, and so forth.

2) Ethanolamine derivatives of the type:

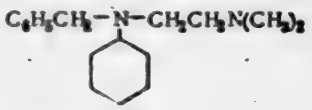


$COCH_2CH_2N(R'''')_2$, where $R' = C_6H_5$; $R'' = C_6H_5CH_2$, $R\text{-}CH_3OC_6H_4CH_2$, cyclohexyl; $R''' = H$, CH_3; $R'''' = CH_3$ or $N(R'''')_2$ = a pyridine group, morpholine, and so forth.

Derivatives of asymmetrically-substituted ethylenediamine with the pyridine ring as substituent R'' are considerably more active than compounds with the phenyl radical as R''. Thus, for example, pyribenzamine (A) is many times more active than anthergane (B):

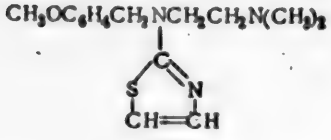


(A)



(B)

In some medicinal preparations, for example, in sulfidine, the pyridine radical can be successfully replaced by the thiazole radical, while at the same time less toxic compounds result. It was therefore of interest to the authors to synthesize a number of new substances analogous to those of known antihistaminics of the ethylenediamine series, in which the pyridine radical would be replaced by the thiazole radical.



(C)

When the authors started their work, there were no compounds described in the literature that contained the thiazole ring in the molecule of an asymmetrically-substituted ethylenediamine. Such ethylenediamine derivatives are now known [1,2].

There exists indication that N,N-dimethyl-N'-(p-methoxybenzyl)-N'-(2-thiazolyl)-ethylenediamine (C) possesses powerful antihistaminic action.

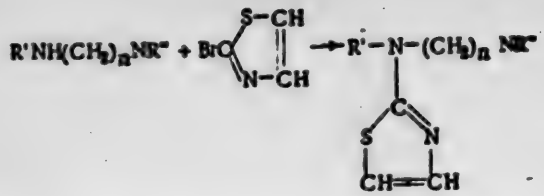
The following procedure was set up for the synthesis of thiazolyl derivatives of ethylene- and trimethyleth-ylene-diamine derivatives.

1. To condense the primary aryl or aralkylamines with dialkylaminoalkylbromides to obtain secondary dialkylaminoalkylaryl (or aralkyl) amines according to the scheme:

$$R'NH_2 + Br(CH_2)_nNR'' \rightarrow R'NH(CH_2)_n\,NR''.$$

where $R' = C_6H_5$, $C_6H_5CH_2$; $R'' = CH_3$ or $N(R'')_2$ = piperidyl; $n = 2$ or 3.

2. To condense with 2-bromthiazole in pyridine according to the scheme:



The author has obtained a series of secondary dialkylaminoalkyl- or aralkylamines, as given in the table. (I) was obtained according to the method given for it in the literature [4]. Preparation (V) has been synthesized for the first time from N-benzyl-benzamide [5]; the author obtained it, in a manner similar to preceding preparation (I), from benzylamine and the hydrobromide of dimethylaminoethylbromide in the presence of potash, in 30% yield of theoretical. Preparation (VI) was obtained by condensing γ-dimethylaminopropylamine with p-methoxybenzylchloride in pyridine.

The secondary amides were colorless liquids, with the exception of preparation (IV), melting at 44°. They formed nicely-crystallizing dihydrochlorides on treatment with the calculated quantity of hydrogen chloride in ether solution.

Preparations (III) and (IV), having electronegative substituents in the para-position of the benzene ring, form only the monohydrochlorides and monopicrates. This is apparently explained by the fact that electronegative substituents in the para-position weaken the basicity of the nitrogen atom bound to the benzene ring, with resulting loss in ability to add a proton; the salt is therefore only formed by the dimethylamino group.

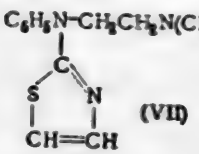
TABLE

preparation no.	structure	boiling point	yield (%)	melting point		empirical formula
				dihycrochloride	picrate	
(I)	$C_6H_5NHCH_2CH_2N(CH_3)_2$	100-105°(6 mm)	70	176-177°	–	–
(II)	$p\text{-}C_2H_5OC_6H_4NHCH_2CH_2NC_5H_{10}$	173-175°(3 mm)	60	174	–	$C_{15}H_{24}ON_2 \cdot 2HCl$
(III)	$p\text{-}C_2H_5COOC_6H_4NHCH_2CH_2N(CH_3)_2$	181-185° (4 mm)	32	Monohydrochloride 159-161	137-138°	$C_{19}H_{23}O_9N_5$ (picrate)
(IV)	$p\text{-}BrC_6H_4NHCH_2CH_2NC_5H_{10}$	180-181°(4 mm) m.p. 44°	32	Monohydrochloride 208	–	$C_{13}H_{19}N_2Br \cdot HCl$
(V)	$C_6H_5CH_2NHCH_2CH_2N(CH_3)_2$	115-117°(4 mm)	30	205-207	–	–
(VI)	$p\text{-}CH_3OC_6H_4CH_2NHCH_2CH_2CH_2N(CH_3)_2$	155-160°(4 mm)	43	188-189	–	$C_{13}H_{22}ON_2 \cdot 2HCl$

Upon boiling dialkylaminoalkylarylamines with 2-bromothiazole in pyridine, derivatives of ethylene- and trimethylenediamine are formed with thiazole radicals as substituents. Small yields result. In synthesis of the analogous pyridine derivatives, it is possible to increase the yield by using an excess of the secondary amine [6]. In the case of the thiazole derivatives this is ineffective.

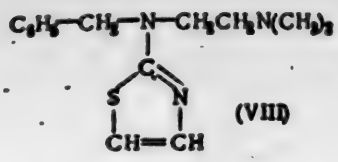
Upon fractionally distilling the reaction mixture in vacuo, the condensation product did not result in pure form; the author therefore purified the bases by means of the perchlorates. Thus, the following preparations resulted:

1. N,N-Dimethyl-N'-phenyl-N'-(2-thiazolyl)ethyenediamine (VII):

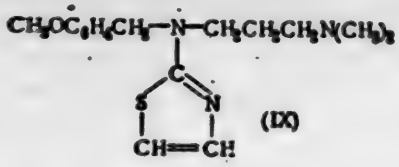


(VII)

2. N,N-Dimethyl-N'-benzyl-N'-(2-thiazolyl)-ethylenediamine (VIII); 3. N,N-Dimethyl-N'-(p-methoxybenzyl)-N'-(2-thiazolyl)-trimethylenediamine (IX): (see top of next page)



(VIII)

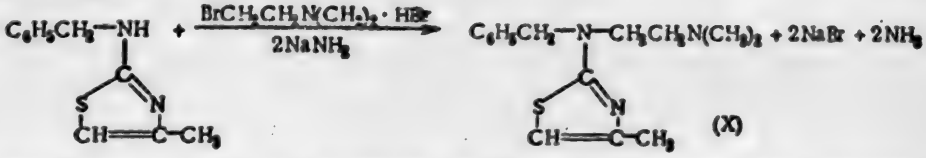


(IX)

Under the conditions indicated (boiling in pyridine), N,N-dimethyl-N'-(carbethoxyphenyl)-ethylenediamine (III) and N-(β-piperidinoethyl)-p-bromoaniline (IV) do not condense with 2-bromothiazole.

The conclusion might be drawn therefore that the mobility of the hydrogen atom of the secondary amino group bound to the benzene ring, in the para position of which is present a negative substituent, decreases sharply.

Upon interacting the hydrobromide of dimethylaminoethylbromide with 2-benzylamino-4-methylthiazole, there resulted accordingly, N,N-dimethyl-N'-benzyl-2-(4-methylthiazolyl)-ethylenediamine (X), in conformity with the equation:



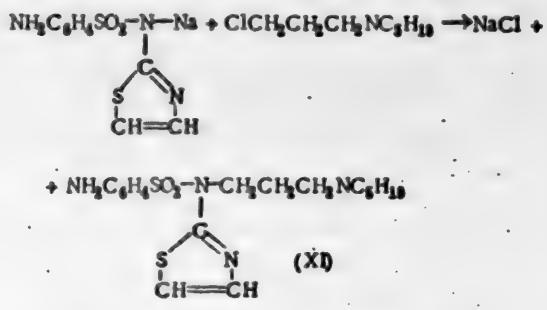
(X)

The yield was negligible. The reaction product was identified in the form of the perchlorate with m.p. 144°.

TABLE

Nitrogen (in %)		Chlorine (in %)	
Found	Calculated	Found	Calculated
–	–	–	–
8.95, 8.96	8.72	–	–
14.82, 14.97	15.05	Monohydrochloride	
		12.97, 12.95	13.12
9.00, 9.13	8.80	11.10, 11.31	11.11
–	–	–	–
9.56, 9.62	9.49	23.91, 23.92	24.06

Upon boiling the sodium salt of 2-p-aminobenzenesulfamidothiazole with γ-piperidinopropylchloride, preparation (XI) resulted in almost quantitative yield, according to the equation:



(XI)

Preparations (VII), (X), and (XI) were tested pharmacologically. It was found that they all possessed antihistaminic action to a greater or lesser degree. The most active was found to be preparation (X), which seems to be the exact analog of pyribenzamine (A). However, the activity of (X) is considerably weaker than that of pyribenzamine.

EXPERIMENTAL

I. Synthesis of the Original Substances.

Hydrobromide of dimethylaminoethylbromide. This was obtained by the method proposed for the hydrobromide of β-bromoethylamine [7]. The crude product was obtained from 142.4 g of dimethylaminoethanol and 700 ml of hydrobromic acid of specific gravity 1.42. The solid residue remaining in the flask after distilling off the hydrobromic acid was thoroughly ground with 350 ml of acetone, filtered off, washed with a small quantity of cooled acetone and dried with ether. The yield was 297 g, 80% of theoretical; m.p. 289°.

Hydrochloride of β-piperidinoethylchloride. This was obtained from piperidinoethanol and thionyl chloride in chloroform solution [8]; m.p. 226-231°.

γ-Piperidinopropylchloride. Obtained from trimethylenechlorobromide and piperidine in ether solution [9]. Distilled at 68-70° and 4 mm.

p-Methoxybenzylchloride. Obtained from anisole, formalin and gaseous hydrogen chloride in the presence of zinc chloride [10]; b.p. 105-110° at 8 mm (literature data 115-120° at 16 mm).

2-Bromothiazole. Obtained by dinitration of 2-aminothiazole in phosphoric acid medium in the presence of nitric acid, with subsequent decomposition of the diazo solution, according to Sandmeyer [11]. Distilled at 74° and 22 mm (literature data, b.p. 69° at 16 mm [11]).

2-Benzylamino-4-methylthiazole [12]. Obtained by condensation of benzylthiourea with chloroacetone. A mixture of 5 g of benzylthiourea and 2.5 ml of chloroacetone (excess) was heated on a water bath for 1 hour. The reaction product was then dissolved in water, and excess chloroacetone extracted with ether. The aqueous solution was alkalized with 10% caustic soda solution, and the precipitated 2-benzylamino-4-methylthiazole was filtered off, washed with water and recrystallized from aqueous methyl alcohol. M.p. 98°; picrate m.p. 192-194°; which corresponded to the literature data. Yield 5.5 g; 90% of theoretical.

The same product was obtained by condensation of 2-amino-4-methylthiazole with benzyl chloride. The yield amounted to 15% of the theoretical.

II. Synthesis of Secondary Dialkylaminoalkylaryl-(aralkyl)-amines.

N-β-Piperidinethyl-p-phenetidine (II). A mixture of 27.4 g of p-phenetidine, 18.4 g of the hydrochloride of β-piperidinoethylchloride and 27.6 g of anhydrous potash in 100 ml of toluene was boiled, with stirring, for 8 hours. After cooling, water was added to dissolve the precipitate, the toluene layer was separated, and the aqueous layer was extracted 3 times with ether. The combined extractions were dried with anhydrous potash, and after distilling off the solvents, the residue was distilled in vacuo with a spiral dephlegmator. The excess p-phenetidine distilled off first, and then the secondary amine was collected at 173-175° and 3 mm. The yield was 14.8 g, 60% of theoretical.

The dihydrochloride resulted on dissolving the amine in absolute ether and adding to the solution the calculated quantity of hydrogen chloride in ether solution. The white precipitate which formed was recrystallized from absolute alcohol; m.p. 174°.

In a similar fashion preparations (I), (III), (IV) and (V) were obtained. N,N-Dimethyl-N'-phenylethylenediamine (I) distilled at 100-105° at 6 mm, which coincides with the data of Leonard and Solmssen [4]. Huttrer and co-workers [13] who obtained this compound for the first time indicated a b.p. of 103-107° at 0.2 mm.

N-N-Dimethyl-N'-(p-methoxybenzyl)-trimethylenediamine (VI). 12.6 g of freshly-distilled p-methoxybenzylchloride was added to a solution of γ-dimethylaminopropylamine in 20 ml of pyridine. After 15 hours boiling, 15 g of solid caustic soda was added and the mixture was heated for another 30 minutes on a water bath, and then filtered. Pyridine was distilled out of the filtrate, and the residue was redistilled in vacuo. The 155-160° at 4 mm fraction was collected. There remained in the distilling flask some higher-boiling liquid, which decomposed upon distillation. Yield was 9.5 g, 45% of theoretical.

The dihydrochloride was obtained as with the preceding; m.p. 188-189°.

III. Synthesis of 2-Thiazolyl Derivatives of Ethylene- and Trimethylenediamine.

N,N-Dimethyl-N'-phenyl-N-(2-thiazolyl)-ethylenediamine (VII). 5.5 g of 2-bromothiazole was added to a solution of 5.5 g of N,N-dimethyl-N'-phenylethylenediamine (I) in 10 ml of pyridine, and the mixture was boiled on reflux for 12 hours. 10 g of solid caustic soda was then added and the mixture boiled on a water bath for 20 minutes. The solution was filtered off from the solid residue, and after distilling off the pyridine, the residue was redistilled in vacuo. The fraction boiling at 145-150° at 5 mm was collected. Yield was 1.45 g. An almost colorless liquid. Gave a perchlorate which was recrystallized from alcohol, m.p. 199°.

Found %: N 8.89, 8.95. $C_{13}H_{17}N_3S \cdot HClO_4$. Calculated %: N 9.20.

N,N-Dimethyl-N'-benzyl-N'-(2-thiazolyl)-ethylenediamine (VIII). Obtained from 6.5 g of N,N-dimethyl-N'-benzylethylenediamine (V) and 3.3 g of 2-bromothiazole in a manner similar to the preceding. The fraction boiling at 183-185° at 5 mm was collected. The yield was 2.1 g, 40% of theoretical, calculating on the basis of 2-bromothiazole.

As has already been mentioned, this compound is described in patent [2], where the melting point of the picrate is given. Since the authors could not obtain the picrate in crystalline form, the base was therefore identified in the form of the perchlorate, which, after recrystallization from alcohol, represented colorless needles with m.p. 139°.

Found %: N 11.50, 11.42. $C_{14}H_{19}N_3S \cdot HClO_4$. Calculated %: N 11.61.

N,N-Dimethyl-N'-(p-methoxybenzyl)-(2-thiazolyl)-trimethylenediamine (IX). Obtained from 8.9 g of N,N-dimethyl-N'-(p-methoxybenzyl)-trimethylenediamine (VI) and 3.2 g of 2-bromothiazole in pyridine, similarly to the preceding. After distilling off the solvent, the residue was redistilled in vacuo at 3 mm. The resulting fractions: I) 155-160°—5.1 g (initial analysis); II) 160-170°—0.5 g; III) 170-195°—2.2 g. The third fraction was redistilled in vacuo once more, and the portion boiling at 185°-190° at 3 mm was collected.

Unfortunately, the author failed to obtain the crystalline hydrochloride; picrate or perchlorate. Analysis of the distillation product gave low nitrogen and sulfur content. Likewise, the condensation product from N-(β-piperidinoethyl)-p-phenetidine and 2-bromothiazole failed to separate in the pure form.

N,N-Dimethyl-N'-benzyl-N'-2-(4-methylthiazolyl)-ethylenediamine. (X). A mixture of 9.6 g of 2-benzylamino-4-methylthiazole and 4.6 g of sodamide in 75 ml of toluene was boiled for 2 hours. 14 g of the hydrobromide of dimethylaminoethylbromide was added to the cooled solution, and the mixture was boiled for another 12 hours. After cooling, the precipitate was filtered off, the toluene distilled off, and the residue distilled in vacuo at 10 mm. Everything distilled in the range 173-195°. It failed to separate into fractions, the distillate being a very thick viscous mass. Upon treating the distillate with 30% chloric acid, it was possible to separate the perchlorate in the form of large prisms, readily soluble in hot alcohol and water. After recrystallization from alcohol, the perchlorate had a m.p. of 144°.

Found %: N 10.98, 10.91; S 8.75, 8.91; Cl 9.29, 9.36. $C_{13}H_{21}N_3S \cdot HClO_4$. Calculated %: N 11.18; S 8.52; Cl 9.45.

Upon action of aqueous sodium carbonate solution on the perchlorate, the base separated out in the form of a colorless oily liquid. It was extracted with ether, the ether extract dried with sodium sulfate, and after distilling off the ether, the oil did not crystallize. The oil dissolved in absolute ether, and to the solution was added the calculated quantity of hydrogen chloride in ether. The resulting precipitate was filtered off rapidly, washed with ether and dried in a vacuum desiccator. The resulting dihydrochloride was very hygroscopic.

N-(2-Thiazolyl)-N-(γ-piperidinopropyl)-p-aminobenzenesulfamide (XI). 3.2 g of γ-piperidinopropylchloride was added to an alcoholic solution of 5.55 g of the sodium salt of 2-(p-aminobenzenesulfamide)-thiazole and the mixture heated for 3 hours. The resulting sodium chloride precipitate was filtered off, and the alcohol was distilled off from the filtrate. The residue was recrystallized from alcohol: m.p. 189°. Yield almost quantitative.

Found %: N 14.86, 15.01; S 16.86, 17.07. $C_{17}H_{24}O_2N_4S_2$. Calculated %: N 14.73; S 16.84.

The base gave only a monohydrochloride: m.p. 203-205°.

Found %: Chlorine ion 8.61, 8.82. $C_{17}H_{24}O_2N_4S_2 \cdot HCl$. Calculated %: Chloride ion 8.52.

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SUMMARY

1. Four new secondary dialkylaminoalkylarylamines have been synthesized.

2. A symmetrically-substituted ethylene- and trimethylene-diamines, containing the thiazole radical as substituent, have been described.

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THIAZOLYL DERIVATIVES OF ETHYLENE- AND TRIMETHYLENE-DIAMINE. II.

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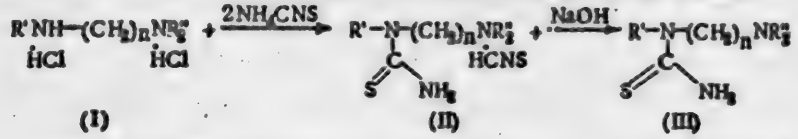
In the preceding work [1] 2-thiazolylsubstituted ethylene- and trimethylene-diamine were described, obtained either by introduction of the thiazole ring into dialkylaminoalkylaryl-(aralkyl)-amine by reacting it with 2-bromothiazole, or by substitution of the hydrogen atom in the aminic group by an alkylaminoalkyl group.

In the present work, synthesis of the thiazole derivatives of ethylene- and trimethylene-diamine has been accomplished in another manner, namely: the dialkylaminoalkyl-(aralkyl)-amine is converted into the dihydrochloride (I), which, upon treating with ammonium rhodanide in chlorobenzene, is converted into the hydrogen rhodanide salt of asymmetric N-aryl-N-[β-dialkylaminoalkyl-(aralkyl)]-thiourea (II), and upon action of the alkali solution on the salt, the free base (III) is separated, according to the scheme:



(I) (II) (III)

Upon interacting equimolecular quantities of the asymmetric N-aryl-N-(β-dialkylaminoalkyl)-thiourea with chloroacetone, cyclization occurs, as the result of which asymmetrically-substituted ethylene- and trimethylene-diamine with the thiazole ring are formed in good yields according to the scheme:

The necessary secondary dialkylaminoalkyl-(or aralkyl) amines used as the intermediate substances for these syntheses were obtained by condensation of aryl or aralkylamines with dialkylaminoalkylbromide (or chloride) in toluene or in alcoholic solution, in the presence of anhydrous potash, as described in the preceding work [1]. Data for the secondary amines obtained are given in Table 1.

Among them compound (III) is described in the literature, and its yield is indicated as 45% of the theoretical [2]; the author has obtained this compound in 63% yield. N,N-Dimethyl-N'-benzyltrimethylenediamine (VI) was obtained by condensation of γ-dimethylaminopropylamine with benzyl chloride in pyridine in a manner similar to that for N,N-dimethyl-N'-(p-methoxybenzyl)-trimethylenediamine described in the preceding work [1]. The dihydrochlorides of the indicated secondary amines resulted on treatment of a solution of the secondary amine in absolute alcohol with the calculated quantity of hydrogen chloride in ether.

Asymmetric derivatives of N-aryl-N-[β-dialkylaminoalkyl- (or aralkyl)]-thiourea are given in Table 2.

They are colorless crystals with melting points below 150°. Poorly soluble in water, readily so in propyl, butyl and isoamyl alcohols. Yields of the recrystallized compounds vary from 23 to 55%.

Asymmetrically-substituted derivatives of ethylene- and trimethylene-diamine, containing the thiazole ring, and resulting from cyclization of asymmetric N-aryl-N-(β-dialkylaminoalkyl)-thioureas with chloroacetone, are given in Table 3.

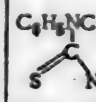
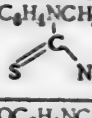
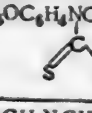
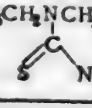
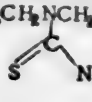
Preparations (XVI), (XVII), (XVIII), (XXII) and (XXIII) represent almost colorless viscous oily liquids with b.p. above 170° at 3 mm. After a certain length of time, they become yellow, and upon standing resinify.

Preparations (XV), (XIX), (XX) and (XXI) are crystalline compounds with m.p. below 100°. All preparations are soluble in organic solvents and do not dissolve in water. Almost all of them give well-formed picrates: exceptions are those compounds which contain the benzyl group. The dihydrochlorides are readily soluble in water. Some of them are very hygroscopic.

TABLE 1

Prep. No.	Structure	B.p.	Yield (%)	M.p. of dihydrochloride	M.p. of picrate	Empirical formula	Nitrogen (%) found	Nitrogen (%) calc.	Chlorine found	Chlorine cal
(I)	$C_6H_5NHCH_2CH_2NC_5H_{10}$	165-167° (4 mm)	76	174-175°	160°	$C_{25}H_{26}O_{14}N_8$ (dipicrate)	16.71	16.91	–	–
(II)	$C_6H_5NHCH_2CH_2CH_2NC_5H_{10}$ . . .	143-145° (3 mm)	80	228-229	–	$C_{14}H_{22}N_2 \cdot 2HCl$	9.76 9.82	9.62	24.12	24.
(III)	$p\text{-}CH_3C_6H_4NHCH_2CH_2N(CH_3)_2$	120-123° (6 mm)	63	175-176	–	$C_{11}H_{18}N_2 \cdot 2HCl$	17.53 17.46	17.61	–	–
(IV)	$p\text{-}CH_3OC_6H_4NHCH_2CH_2N(CH_3)_2$	131-133° (4 mm)	66	165-166	–	$C_{11}H_{18}N_2O \cdot 2HCl$	10.65 10.69	10.48	–	–
(V)	$p\text{-}C_2H_5OC_6H_4NHCH_2CH_2N(CH_3)_2$	133-135° (4 mm)	65	160-161	–	$C_{12}H_{20}N_2O \cdot 2HCl$	9.85 10.03	9.96	24.97 25.26	25.
(VI)	$C_6H_5CH_2NHCH_2CH_2CH_2N(CH_3)_2$	130-133° (6 mm)	53	207	–	$C_{12}H_{20}N_2 \cdot 2HCl$	10.33 10.28	10.56	26.47 26.40	26.

TABLE 2

Prep. No.	Structure	M.p.	Yield (%)	Empirical formula	Nitrogen (%) Found	Nitrogen (%) Calc.	Sulfur (%) Found	Sulfur (%) Calc.
(VII)	$C_6H_5NCH_2CH_2N(CH_3)_2$ 	131-132°	50	$C_{11}H_{17}N_3S$	18.72	18.83	14.49	14.35
(VIII)	$C_6H_5NCH_2CH_2NC_5H_{10}$	114-115	45	$C_{14}H_{21}N_3S$	15.82 15.68	15.96	12.36 12.27	12.16
(IX)	$C_6H_5NCH_2CH_2CH_2NC_5H_{10}$	112	40	$C_{15}H_{23}N_3S$	15.09 14.90	15.16	11.70 11.72	11.55
(X)	$CH_3C_6H_4NCH_2CH_2N(CH_3)_2$ 	130	52	$C_{12}H_{19}N_3S$	17.47 17.42	17.72	13.23	13.50
(XI)	$CH_3OC_6H_4NCH_2CH_2N(CH_3)_2$	146	50	$C_{12}H_{19}ON_3S$	16.49 16.37	16.60	12.92	12.64
(XII)	$C_2H_5OC_6H_4NCH_2CH_2N(CH_3)_2$ 	137-138	55	$C_{13}H_{21}ON_3S$	15.66 15.63	15.72	11.98 12.19	11.98
(XIII)	$C_6H_5CH_2NCH_2CH_2N(CH_3)_2$ 	105	38	$C_{12}H_{19}N_3S$	17.60 17.43	17.72	13.58 13.82	13.52
(XIV)	$C_6H_5CH_2NCH_2CH_2CH_2N(CH_3)_2$ 	102	23	$C_{13}H_{21}N_3S$	16.52 16.61	16.73	12.72 12.95	12.74

Preparation (XXI) resulted from the cyclization of N-(p-ethoxyphenyl)-N-(β-dimethylaminoethyl)-thiourea (XII) with bromoacetophenone. This preparation forms only the monohydrochloride and monohydrobromide. Both salts are very poorly soluble in water. Hence, replacement of the methyl group with the phenyl radical in position 4 of thiazole greatly decreases the solubility of these preparations in water.

The compounds listed in Table 3 were tested pharmacologically. It was found that they possess antihistaminic action, but antihistaminic activity below preparations of practical use.

EXPERIMENTAL

I. Synthesis of Asymmetric N-Aryl-(aralkyl)-N-(β-dialkylaminoalkyl)-thioureas.

As-N-phenyl-N-(β-dimethylaminoethyl)-thiourea (VII). A mixture of 42.6 g of the dihydrochloride of N,N-dimethyl-N'-phenylethylenediamine and 27 g of ammonium rhodanide in 100 ml of chlorobenzene was heated on a boiling water bath with mechanical stirring for 15 hours. The resulting yellow precipitate was filtered off, washed with a small quantity of ice water, and then dissolved in hot water. The solution was treated with activated carbon and filtered. From the filtrate there precipitated after a given length of time pretty white needles. The yield was 20.3 g = 50% of theoretical. The crystals, recrystallized from butyl alcohol, had a m.p. of 169-170° and gave a positive reaction for the rhodanide ion with a solution of iron chloride.

An analysis for nitrogen and sulfur confirmed the formation of the hydrorhodanide salt of asymmetrical thiourea, from which sodium carbonate does not liberate the free base.

Found %: N 19.92, 19.61; S 22.50, 22.62. $C_{12}H_{18}N_4S_2$. Calculated %: N 19.85; S 22.69.

The thiourea base resulted from a processing of the hydrorhodanide salt with 10% caustic soda solution. The base, recrystallized from butyl alcohol, melted at 131-132°.

The hydrochloride salt of thiourea resulted in quantitative yield on combining an ether solution of thiourea with an alcoholic solution of hydrogen chloride. M.p. of the hydrochloride salt was 199°.

Preparations (VIII)-(XIV) were obtained in a similar fashion.

As was to be expected, the secondary dialkylaminoalkylarylamines containing negative substituents in the para-position of the phenyl ring, and which formed only the monohydrochlorides (N,N-dimethyl-N'-(p-carbethoxyphenyl)-ethylenediamine and N-(β-piperidinoethyl)-p-bromoaniline [1]) did not form thiourea derivatives.

II. Synthesis of Thiazolyl derivatives of Ethylene- and Trimethylenediamine.

N,N-Dimethyl-N'-phenyl-N'-2-(4-thiazolyl)-ethylenediamine (XV). 5 ml of chloroacetone (excess) was added to 4.6 g of as-N-phenyl-N-(β-dimethylaminoethyl)-thiourea (VII). After several minutes, a strong evolution of heat was observed, and the reaction mixture liquified. To complete reaction, the mixture was heated an additional hour on a water bath at 80-90°, was then dissolved in water, and the excess of chloroacetone was extracted with ether two times with 5 ml portions.

The aqueous solution was alkalized with caustic soda solution and was extracted three times with 10 ml portions of ether. The ether extract was dried with calcined potash, and after distilling off the ether, the remaining oil crystallized after a certain time. The crystals were dissolved in absolute ether, treated with activated carbon, filtered, and after evaporating the ether off, the remaining light-yellow crystals had a m.p. of 61-62°. Yield was 5.1 g.

If instead of the thiourea base, its hydrochloride or hydrorhodanide salt is used for condensation with chloroacetone, the same product in the same yield results.

The picrate was recrystallized from alcohol. M.p. 185°.

Found %: N 16.89, 17.07. $C_{19}H_{22}O_7N_6S$. Calculated %: N 17.14.

The dihydrochloride was obtained by addition of the calculated quantity of hydrogen chloride in ether solution to the basic solution in absolute alcohol.

Recrystallized from a mixture of absolute alcohol and ether. M.p. 192°. Readily soluble in water.

All preparations given in Table 3 were obtained similarly.

TABLE 3

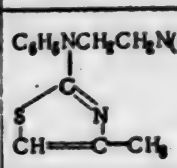
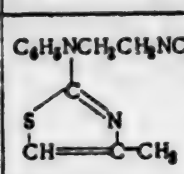
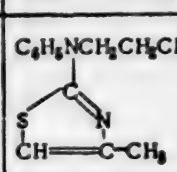
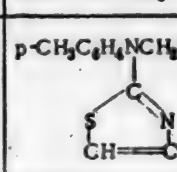
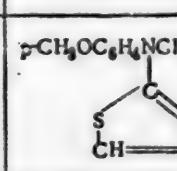
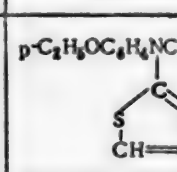
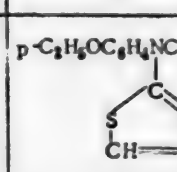
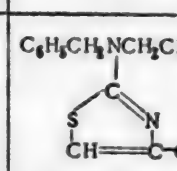
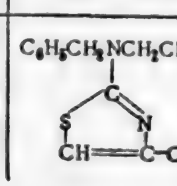
Prep. No.	Structure	Boiling point	Melting point	Yield (%)	M.p. of the dipicrate
(XV)		–	61-62°	95	165°
(XVI)		180-183° (4 mm)	–	76	179
(XVII)		Not distilled	–	85	185
(XVIII)		170-173° (4 mm)	–	84	189
(XIX)		–	47-48	91	201
(XX)		–	68.5	78	192 (with decomp.)
(XXI)		–	59	–	Monohydrobromide 213-215°
(XXII)		171-174° (3 mm)	–	82	Perchlorate m.p. 144°
(XXIII)		180-182° (3 mm)	–	84	177°

TABLE 3

M.p. of the dihydrochloride	Empirical formula	Nitrogen (%)		Sulfur (%)		Chlorine (%)	
		Found	Calculated	Found	Calculated	Found	Calculated
192°	$C_{16}H_{19}N_3S$	15.93 15.98	16.08	12.39 12.35	12.26	–	–
hygroscopic	$C_{29}H_{29}O_{14}N_9S$ (dipicrate)	16.76 16.61	16.62	4.52	4.21	–	–
164°	$C_{30}H_{31}O_{14}N_9S$ (dipicrate)	16.30 16.18	16.30	4.02 4.28	4.13	–	–
hygroscopic	$C_{27}H_{37}O_{14}N_9S$ (dipicrate)	17.32 17.41	17.19	4.37 4.46	4.36	–	–
144-145°	$C_{27}H_{27}O_{13}N_9S$ (dipicrate)	16.64 16.74	16.82	4.27	4.35	–	–
139-140° (with decomp.)	$C_{28}H_{29}O_{13}N_9S$ (dipicrate)	16.24 16.17	16.48	4.21 4.25	4.19	–	–
–	$C_{21}H_{25}ON_3S \cdot HBr$	9.16 9.23	9.37	7.36	7.14	Monohydrochloride 9.00 9.13	8.82

Identical with preparation (X) described in the preceding work [1].

hygroscopic	$C_{28}H_{29}O_{14}N_9S$ (dipicrate)	16.71 16.66	16.85	4.24 4.21	4.28	–	–

Those preparations which did not crystallize after distilling off the ether (XVI, XVII, XVIII, XXII, XXIII) were redistilled in vacuo and identified in the form of the dipicrates.

N, N-Dimethyl-N'-benzyl-N'-2-(4-methylthiazolyl)-ethylenediamine (XXII) was obtained from the as-N-benzyl-N-(β-dimethylaminoethyl)-thiourea and chloroacetone, and after the usual treatment was redistilled in vacuo at 183-185° at 3 mm. The yield was 84% of theoretical. A light-yellow, viscous, oily liquid which formed the perchlorate upon treatment with a 30% solution of chloric acid. After recrystallization from alcohol, the perchlorate represented colorless needles with m.p. 144°. This perchlorate was found to be identical with the perchlorate obtained by the author upon treatment with chloric acid of the condensation product between 2-benzylamine-4-methylthiazole and dimethylaminoethylbromide in the presence of sodamide [1]. A mixed sample of the two perchlorates did not give depression.

The author duly acknowledges the valuable directions on the work by Professor A. I. Kiprianov, Active Member of the Ukrainian SSR Academy of Science.

SUMMARY

1. Eight asymmetrical N-aryl-(aralkyl)-N-(β-dialkylaminoalkyl)-thioureas have been obtained from the condensation of secondary dialkylaminoalkylaryl- (or aralkyl)amines with ammonium rhodanide.

2. Eight corresponding asymmetrically-substituted ethylene- and trimethylene-diamines, with the thiazole ring as substituent, have been isolated from condensation of the resulting asymmetric thioureas with chloroacetone.

LITERATURE CITED

[1] S. G. Fridman, J. Gen. Chem., 23, 278 (1953). •

[2] F. Willani, N. Sperber, J. Lang, D. Papa, J. Am. Chem. Soc., 72, 2724 (1950).

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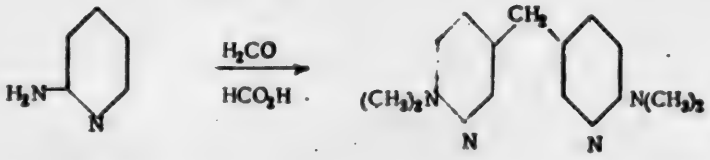
• See Consultants Bureau English translation, page 291.

THE MECHANISM OF METHYLATION OF α-AMINOPYRIDINE ACCORDING TO LEUCKART, AND THE CONDENSATION OF DIMETHYLAMINOPYRIDINE WITH FORMALDEHYDE

A. I. Titov and A. N. Baryshnikova

In 1929 A. E. Chichibabin and I. L. Knunyants [1] discovered an interesting synthesis of tetramethyldiaminodipyridylmethane, heating α-aminopyridine with a mixture of formaldehyde and formic acid solution:



The authors studied the factors of dilution and of gradual addition of α-aminopyridine in the Chichibabin-Knunyants' reaction in the hope of obtaining compounds with but one aminopyridine radical. The authors' assumption was found to be true – from the reaction product under the conditions given dimethylaminopyridine and the hitherto unknown 2-dimethylaminopyridine-5-carbinol were isolated:

Further experimental work allowed the assumption that the Chichibabin-Knunyants reaction starts with a rapid formation of condensation products between formaldehyde and the amino group of α-aminopyridine. Among them, the authors have succeeded in isolating for the first time in crystalline form methyldi-(2-aminopyridine) $C_5H_4N-NH-CH_2-NH-C_5H_4N$. The remaining products of this reaction represent compounds of the same type $C_5H_4N-NH-CH_2OH$, $C_5H_4N-N=CH_2$ and its polymers, since upon their treatment with a mixture of dilute acids, they are easily restored to aminopyridine.

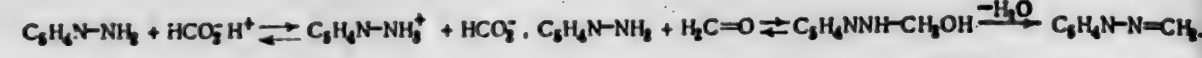
In addition, these products convert into methyl- and dimethylpyridine under the action of formic acid and the formate ion. An optimum acidity for the reaction exists – it does not proceed in a neutral medium or when considerable amounts of mineral acid are added.

Furthermore, dimethylaminopyridine condenses with formaldehyde to form dimethylaminopyridylcarbinol (I), and the latter with a second amine molecule to tetramethyldiaminodipyridylmethane (V). For both condensation reactions an optimum acidity was observed. From several indications (high polarity of the medium and of the reagents, catalysis by hydrogen ion, existence of an acidity optimum) it can be concluded that all of the transformations observed are of a complex ion character. The authors therefore considered that the following fundamental conditions for a complex ion process are realized in all of the transformations as formulated earlier by the authors [2]:

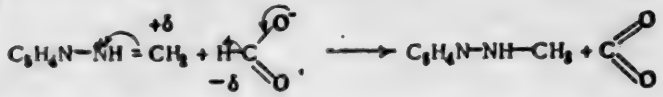
1) the appearance of opposite charges (+δ and −δ) of the directly interacting atoms, and the possibility for their increase at the expense of bond polarization;

2) unsaturated coordination (spherical accessibility) for the directly reacting atoms.

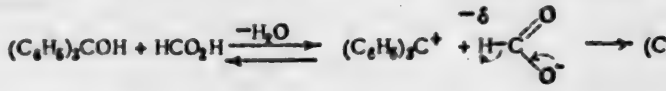
In conformity with this postulate, and with the experimental data, the mechanism of formation of methyl- and of dimethyl-aminopyridine appears to the authors to be as follows. At first the attainment of reaction equilibrium is reached rapidly at the expense of interaction of the amino group with a proton and with formaldehyde, with resulting formation of the methylol bases, anil, dianil [methylene-di-(2-aminopyridine)] and methylene-pyridylammonia, which do not require particular explanations:



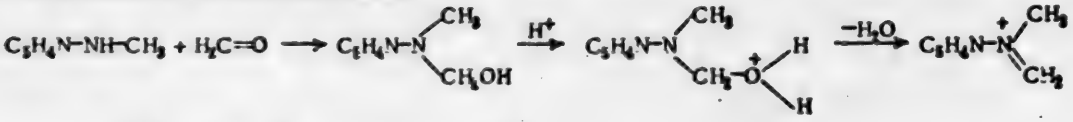
According to our concept and observations concerning the evolution of CO_2 in this reaction, the formation of methylaminopyridine should of course be accompanied by reduction of the methylenepyridylammonia cation by the formate ion:

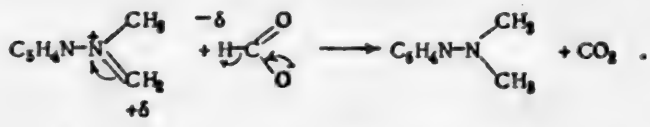


Similar examples of the analogous action of formate ion are the reductions of mercury, silver, and finally triphenylcarbinol cations. The mechanism of the last process may be represented by the scheme:



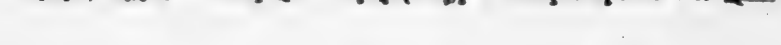
The development of a concept on the mechanism is pertinent to an understanding of the various modifications of the Leuckart reaction, and other similarly-related processes. The formation of dimethylaminopyridine will be presented by the following scheme:

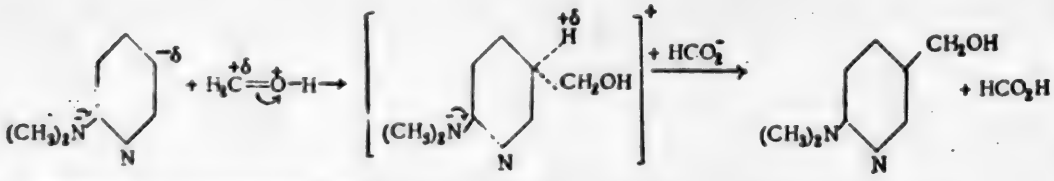




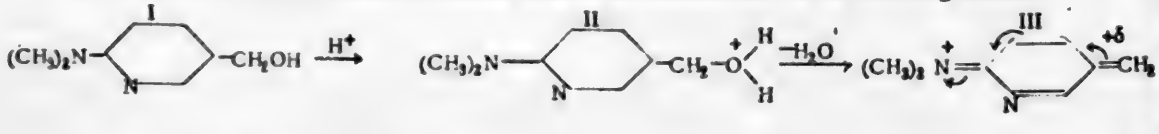
In contrast to the usual ionic reaction, the reduction of methyleneammonium cation by formate ion requires a corresponding orientation and activation energy for the ions.

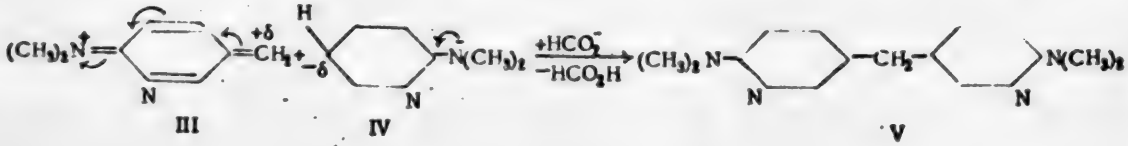
For an understanding of the following condensation, it is important to mention that the optimum pH value also lies in the range of solution acidity given by formic acid-formate mixtures. This circumstance, together with the earlier-indicated conditions for reaction of the complex ion, leads to the following mechanism of formation of dimethylaminopyridylcarbinol:





The authors present the course of the second stage of the condensation in the following manner:





III IV V

Dimethylaminopyridylcarbinol (I), along with the normal cation of the ammonium type, forms with the hydrogen ion an oxonium cation (II); the latter by splitting out water converts into the anhydro cation (III). Cation (III) (second line) reacts with free dimethylaminopyridine (IV), which leads to the formation of tetramethyldiaminodipyridylmethane (V); the splitting off of a proton from the transition complex (not shown in the scheme) occurs as in the preceding condensation, with formate anion participating.

In conformity with the understanding of the Chichibabin-Khunyants' reaction mechanism, by making use of added potassium formate, the authors succeeded in synthesizing tetramethyldiaminodipyridylmethane from aminopyridine in a very short time.

EXPERIMENTAL

Synthesis of Methylene-bis-(2-aminopyridine). a) 10 g of α-aminopyridine was dissolved in 20 ml of alcohol, 30 ml of formaldehyde was added to the solution rapidly, and then 40 ml of 40% NaOH. Heat was evolved. After cooling, it was extracted with ether and dried with potash. Upon slow evaporation of the ether, large colorless, prismatic crystals separated, with m.p. 120°. 7 g of pure product was isolated.

0.736 mg substance: 1.803 ml N_2 (23°, 745.6 mm). Found %: N 27.80. $C_{11}H_{12}N_4$. Calculated %: N 27.92.

The solubility of the product in water, even with heating, was very small; for its recrystallization, it is convenient to carry out same from acetone. Upon heating with dilute mineral acids, hydrolysis proceeded with separation of formaldehyde.

b) 10 g of α-aminopyridine and 3.5 g of paraform were heated in an open flask on a paraffin bath for 30 minutes at 120°, and for an additional 30 minutes at 150°. The loss in weight constituted 3.3 g. The residue in the flask crystallized from acetone, about 4 g of crystalline product resulting, which was identical with that described above.

Synthesis of Dimethyl-2-aminopyridine and Dimethyl-2-aminopyridyl-5-carbinol from 2-Aminopyridine. 150 ml of 20% formalin, turbid because of polymer content, and 50 ml of 90% formic acid were boiled to transparency and then 15 g of sodium formate was introduced. The solution of 3 g of α-aminopyridine in 10 ml of formic acid was boiled beforehand for 2 hours to make the formyl derivative, and was then added gradually, dropwise, to the mixture over a period of 3 hours, with reflux boiling. After the mixing, boiling was continued for an additional 3 hours. Then, to remove the possibility of further condensation reaction, 12 ml of concentrated sulfuric acid was added to the reaction mass and the latter distilled on an oil bath until the temperature of the residue in the flask reached 120°. The residue in the flask was alkalized, and the bases were extracted with ether. The extraction was dried with potash and after the usual preliminary operations was fractionally distilled in vacuo (5 mm).

The following fractions resulted: I) 67-70°—1.65 g; II) 140-160°—1.06 g; III) 180-220°—0.36 g.

The first fraction consisted principally of dimethylaminopyridine, as was established by determination of the boiling point, and by conversion into the picrate and into the nitro compound; they did not depress the melting point when heated with products of known structure.

The second fraction, boiling at about 155°, partially crystallized upon seeding with earlier-obtained dimethylaminopyridylcarbinol. After recrystallization from petroleum ether, the product was obtained as large crystals with m.p. 46°.

1.829 mg substance: 0.304 ml N_2 (27°, 732 mm). Found %: N 18.31. $C_8H_{12}ON_2$. Calculated %: N 18.43.

Small quantities of the carbinol can be separated and identified with the aid of the aurate, m.p. 146-147°.

2.346 mg substance: 0.1216 ml N_2 (24°, 729 mm). Found %: N 5.72. $C_8H_{13}ON_2Cl_4Au$. Calculated %: N 5.58.

The aurate of dimethylaminopyridine, which we have not described before, melts at 155-156°, and the tetramethyldiaminodipyridylmethane at 168-169°.

The chosen structure for dimethylaminopyridylcarbinol was proved by converting it into Chichibabin-Khunyants' tetramethyldiaminodipyridylmethane (experiment 3) by reaction with dimethylaminopyridine.

The third fraction also crystallized upon standing. After recrystallization from petroleum ether, there resulted a little of the pure tetramethyldiaminodipyridylmethane.

Condensation of Dimethylaminopyridylcarbinol with Dimethylaminopyridine. A mixture of 0.2 g of carbinol, 0.5 g of dimethylaminopyridine, 1 ml of 80% formic acid and 1 ml of water was heated for 10 hours at 100°. The reaction mass was evaporated on a water bath, and after alkalization, was redistilled with steam. The remaining oil (0.[illegible] g) after seeding with tetramethyldiaminodipyridylmethane, crystallized. The melting point of the resulting product was 74-76°, and upon heating a mixed sample with known tetramethyldiaminodipyridylmethane an increase in m.p. to 78° was observed.

Under similar conditions a condensation product of carbinol with dimethylaniline was obtained, with a m.p. of 80°. Upon using hydrochloric acid instead of formic acid, condensation did not proceed.

Condensation of Dimethylaminopyridine with Formaldehyde.

Synthesis of Dimethylaminopyridylcarbinol. A mixture of 3 g of dimethylaminopyridine, 15 ml of 20% formaldehyde solution, 8 ml of formic acid and 3 ml of concentrated sulfuric acid was boiled for 19 hours on a reflux. 3.24 g of product resulted after alkalization, extraction with ether and distilling off the solvent from the extract. Redistillation at 5 mm pressure gave the following fractions: I 155-156°—1.23g; II 220-240°—1.22 g; the residue was 0.8 g.

The first fraction was very pure dimethylaminopyridylcarbinol, the second—tetramethyldiaminodipyridylmethane.

Synthesis of Tetramethyldiaminodipyridylmethane from Aminopyridine or Dimethylaminopyridine. A mixture of 3 g of aminopyridine, 8 ml of 90% formic acid, 15 ml of 20% formaldehyde solution and 6 g of potassium formate was boiled for 4 hours under a reflux condenser. The excess of formic acid and formalin was distilled off from the reaction mass on an oil bath until the temperature in the flask reached 150°. The residue in the flask was alkalized and extracted with ether; the extract was dried with potash. 3.6 g of the product resulted from the ether extract after distillation, upon fractionation of this product at 6 mm pressure, the following distillates resulted: I 200-240°—2.6 g; II 240-280°—0.5 g.

The first fraction crystallized completely and consisted of quite pure tetramethyldiaminodipyridylmethane; the composition of the second fraction was not investigated. If 4 ml of concentrated sulfuric acid is added before distilling on an oil bath, small amounts of dimethylaminopyridine and carbinol will be found. Without adding formate, but adding sulfuric acid, before the beginning of the reaction, a large portion of aminopyridine remains without change.

With dimethylaminopyridine, carrying the reaction out under basic conditions, the yield and quality of product was increased.

SUMMARY

1. 2-Dimethylaminopyridine and 2-dimethylaminopyridyl-5-carbinol have been synthesized on the basis of reaction between 2-aminopyridine and formaldehyde in the presence of formic acid. A procedure for the rapid synthesis of bis-(2-dimethylaminopyridyl-5)-methane (tetramethyldiaminodipyridylmethane) according to the same method has been offered.

2. In the same manner, dimethylaminopyridylcarbinol and tetramethyldiaminodipyridylmethane have been synthesized from dimethylaminopyridine.

3. It has been demonstrated that acidity optima are evident for speed in methylation and condensation of the investigated reaction.

4. A mechanism of methylation of α-aminopyridine according to Leuckard, and of the condensation of dimethyl-aminopyridine with formaldehyde has been proposed and experimentally substantiated.

5 Two new compounds have been described: 2-dimethylaminopyridyl-5-carbinol and methylene-bis-(2-aminopyridine).

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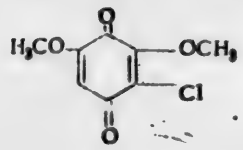
INVESTIGATIONS IN THE FIELD OF QUINONES

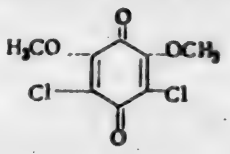
II. CHLORMETHOXYQUINONES

I. S. Ioffe and A. F. Sukhina

Quinone derivatives containing chlorine atoms and methoxyl groups have received but little study up to the present time. Only isolated representatives have been described. Thus, e.g., 3-chloro-2,6-dimethoxyquinone (I) was obtained [1] by passing chlorine through a solution of 2,6-dimethoxyquinone in chloroform. At the same time 3,5-dichloro-2,6-dimethoxyquinone (II) is also formed.



(I)



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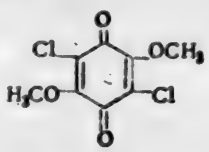

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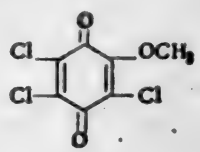

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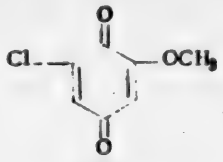
3,5-Dichloro-2,6-dimethoxyquinone (II) is also formed [2] by treating chloroanil with methyl alcohol in the presence of caustic potash; however, with this reaction the main product is found to be 3,6-dichloro-2,5-dimethoxyquinone (III). The latter has also been obtained by methylation of chloroanilic acid with dimethylsulfate [3]. 3,5,6-Trichloro-2-methoxyquinone (IV) has been described, obtained from tetrachlorobenzene [4].

The simpler quinone derivatives which contain only one methoxyl group and one chlorine atom, in particular, 6-chloro-2-methoxyquinone (V) and 5-chloro-2-methoxyquinone (VI) as yet have not been described.



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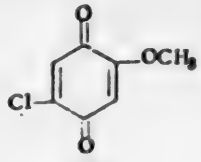
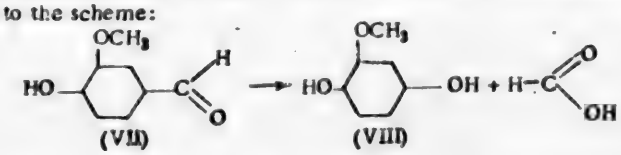


(VI)

The synthesis of these derivatives could be approached in a variety of ways, namely: methoxylation of chloroquinone, chlorination of methoxyquinone, and other means of synthesis from substances already containing chlorine atoms and methoxyl groups in definite positions. The authors synthesized chloromethoxyquinones (V) and (VI) starting with the isomeric chlorovanillins, and utilizing the Dakin reaction [5], which consists of treating o- or p-hydroxyaldehydes with hydrogen peroxide in alkaline solution. This reaction finally leads to breaking of the bond between the aromatic ring and the carbon atom of the aldehyde groups, which splits off as formic acid and is replaced by the hydroxyl group. Diatonic phenol which is produced can, by oxidation, be converted into the corresponding quinone derivative.

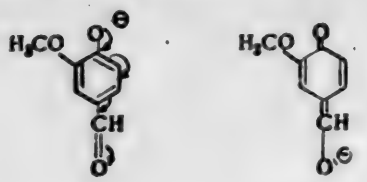
By such a reaction, 2-methoxyquinone, in particular, is formed. Here the initial substance is vanillin (VII), which upon treatment with hydrogen peroxide in alkaline solution is converted into 2-methoxyhydroquinone (VIII) according to the scheme:



(VII) (VIII)

Upon examination of this scheme the question arises as to why the bond between the carbon atoms of the benzene ring and the aldehyde group is so easily broken. It should be taken into account, however, that the Dakin

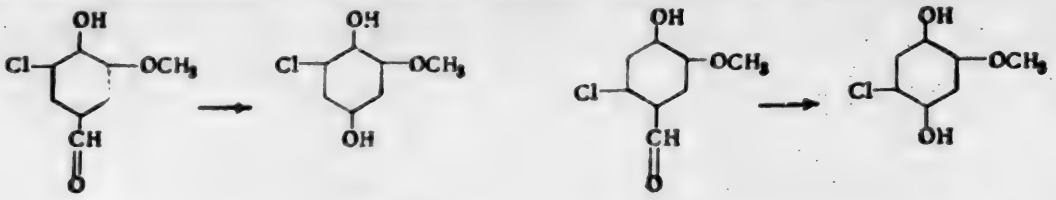
reaction proceeds in alkaline medium, and that in such case, with the hydroxyaldehyde anion, e.g., of vanillin (a) there is displacement of electrons with replacement of the negative charge of the oxygen atom of the carbonyl group (b), with the appearance of the quinoid structure. A certain confirmation of this assumption is the fact that an alkaline solution of vanillin, and of other hydroxyaldehydes containing the hydroxyl groups in the o- or p- position to the carbonyl group, are colored yellow.



(a) (b)

In such a quinoid state a double bond appears between the ring carbon atoms and the carbonyl group, which ruptures under the action of an oxidizing agent.

The isomeric chlorovanillins (IX) and (X) were subjected to the Dakin reaction. 3-Chloro-4-hydroxy-5-methoxybenzaldehyde (IX) resulted from direct chlorination of vanillin in chloroform [6], and separated in the form of colorless needles with m.p. 165°. Upon treating this compound with hydrogen peroxide, in alkaline solution, the authors obtained 6-chloro-2-methoxyhydroquinone (XI), from which, by oxidation, 6-chloro-2-methoxyquinone (V) resulted:



(IX) (XI) (X) (XII)

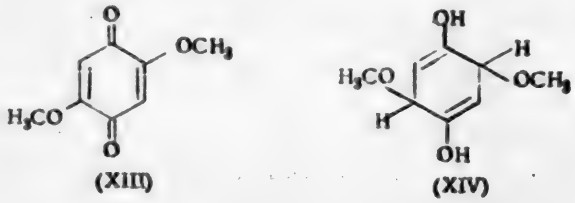
The authors obtained 2-chloro-4-hydroxy-5-methoxybenzaldehyde (X) by chlorination of acetyl vanillin [6], where, because of the hydroxyl group blocking, the chlorine atom entered the ring under the orienting influence of the methoxy group already in the para position to it. After saponification of the acetoxy group, 2-chloro-4-hydroxy-5-methoxybenzaldehyde resulted in the form of colorless crystals, with m.p. 168°. Upon treatment of this compound according to the Dakin reaction, 5-chloro-2-methoxyhydroquinone (XII) resulted, from which, by oxidation, the authors obtained 4-chloro-2-methoxyquinone (VI).

5-Chloro-2-methoxyquinone is somewhat less soluble in alcohol and in acetic acid than the 6-chloro-isomer. Both of the chloromethoxyquinones crystallize in the form of yellow crystals, distinct in their form and melting point. 6-Chloro-2-methoxyquinone crystallizes out from alcohol in the form of thin needle crystals with m.p. 159°; 5-chloro-2-methoxyquinone crystallizes out in the form of plates with m.p. 173°.

The authors also attempted synthesis of the above-described chloromethoxyquinone by methoxylating chloroquinone.

Direct introduction of the methoxyl group into the quinone ring was accomplished for the first time in 1901 by Buckel [7]. Upon heating benzoquinone in methyl alcohol in the presence of anhydrous zinc chloride, he obtained the dimethoxy derivative of quinone, which was identified with the oxidation product of 1,4-diamino-2,5-dimethoxybenzene. It was proved by the same fact that both methoxyl groups entered into the p-position to one another, with formation of 2,5-dimethoxyquinone (XIII).

The latter is obtained from this reaction in a yield of about 33% with regard to the quinone introduced into the reaction. However, this low yield corresponds to that theoretically calculated, it seems, because for each three quinone molecules introduced into reaction, only one can be converted to the 2,5-dimethoxyquinone, the two remaining ones serving to oxidize the primary addition product formed, of possible structure (XIV), transforming at the same time into hydroquinone.



(XIII) (XIV)

The close-to-theoretical yield of 2,5-dimethoxyquinone is explained to a considerable extent by the fact that this compound is not very soluble in organic solvents, methyl alcohol in particular, and therefore, separating as it precipitates, does not decompose under the conditions which are relatively harsh for quinones.

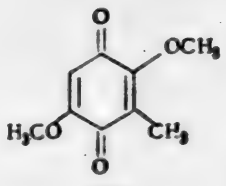
The authors attempted to increase the yield of 2,5-dimethoxyquinone by addition of oxidizing agents into the reaction medium, for example, anhydrous iron chloride or lead peroxide, but they were unsuccessful; it even led to a considerable lowering of the yield, which is evidently related to the action of the oxidizing agent upon the methyl alcohol.

The attempt to synthesize 2,5-dimethoxyquinone in high yield, using monomethoxyquinone prepared by the procedure given before, was unsuccessful [8]. Upon heating the latter with methyl alcohol in the presence of zinc chloride, only traces of 2,5-dimethoxyquinone were obtained. The principal product of the given reaction was found to be the dimer of methoxyquinone, blue-violet in color, and resulting from the action of acid reagents on methoxyquinone.

The formation of such a compound is characterized by coloration of the solution to an intense blue color, which can serve in particular as a qualitiative test for methoxyquinone.

These experiments are of value for a study of the methoxylation reaction mechanism. Up to this point, it seemed possible from these experiments that the synthesis of dimethoxyquinone was preceded by the formation of monoethoxyquinone with its subsequent methoxylation to 2,5-dimethoxyquinone. However, this hypothesis is contradicted by the fact that dimethoxyquinone is formed in good yield, corresponding to theory, and that upon obtaining dimethoxyquinone from quinone, the blue coloration which is characteristic for the dimerization product of monomethoxyquinone does not appear. It seemed more probable, therefore, that formation of 2,5-dimethoxyquinone is preceded by immediate addition of two molecules of methyl alcohol to the quinone molecule, with formation of addition product (XIV) which, upon oxidation, is converted into 2,5-dimethoxyquinone.

The Bückel reaction was also utilized in 1937 [9] for methoxylation of toluquinone. The authors of the work hoped to introduce into the latter molecule two methoxyl groups, with the formation of dimethoxytoluquinone (XV). However, they could only separate 2-methyl-5-methoxyquinone (XVI) – although in small yield.



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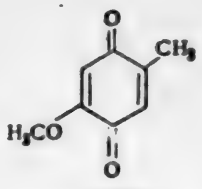

(XVI)

In the present article the authors have methoxylated chloroquinone under conditions of the Bückel reaction, hoping to obtain chloromethoxyquinone. However, the principal reaction product was found to be the 2,5-dimethoxyquinone, identified with the substance resulting directly from quinone. This indicates that under the relatively harsh Bückel reaction conditions heating chloroquinone with methyl alcohol in the presence of zinc chloride along with direct introduction of one methoxyl group into the quinone ring – substitution of chlorine by the second methoxyl group also takes place. Therefore, methoxylation of chloroquinone does not lead to the formation of chloromethoxyquinones.

EXPERIMENTAL

I. Methoxyquinone. 6 g of vanillin was dissolved in 40 ml of 4% caustic soda. To the light-yellow colored solution was added at once 40 ml of 5% hydrogen peroxide solution. Upon this, the solution gave off heat, up to 40°, and darkened. The dark-brown solution was left standing at room temperature for an hour. After 1 hour the solution was acidified with 20% sulfuric acid solution (8 ml), and was immediately placed in a cooling mixture. When the solution temperature had been lowered to −3°, it was added dropwise, with stirring, over a period of two hours, to the oxidizing mixture (40 g of sodium bichromate in 75 ml of 20% sulfuric acid). The oxidizing mixture should be pre-cooled to −5°. The mixture temperature should not exceed 0° during the oxidation. A temperature increase, even to +5°, lowers considerably the yield of methoxyquinone. For this reason it is not recommended that the experiment be carried out under laboratory conditions with large quantities of vanillin, since it is difficult to regulate the reaction temperature.

The methoxyquinone precipitated gradually in the form of fine yellow needles. After completion of the oxidation, the mixture with methoxyquinone precipitate was left standing for 2 hours at 0°, and the precipitate was then filtered off, washed with iced water and dried in a desiccator over calcium chloride. The weight of dry methoxyquinone was 3.4 g. The filtrate was treated several times with ether, the ether distilled off on a water bath, and upon separating of the crystals, the residue was poured into a Petri dish. The weight of dry residue was 0.5 g. The total weight of methoxyquinone was 3.9 g, i.e., 71% of the theoretical, calculating on vanillin. After recrystallizing from alcohol – light-yellow needle crystals, with m.p. 144°. Readily soluble in alcohol, ether, chloroform, glacial acetic acid and poorly soluble in water.

II. 6-Chloro-2-methoxyquinone. 3-Chloro-4-hydroxy-5-methoxybenzaldehyde resulted from the direct chlorination of vanillin in chloroform [6] and was separated in the form of colorless crystals with m.p. 165°.

6 g of 3-chloro-4-hydroxy-5-methoxybenzaldehyde was dissolved in 40 ml of 4% caustic soda. To the dark yellow colored solution, 40 ml of 5% hydrogen peroxide solution was added at once. The solution heated up to 40° and darkened. The dark brown solution was left standing for 30-40 minutes at room temperature. After 30 minutes the solution was acidified with 20% sulfuric acid solution (8 ml) and placed in a cooling mixture. At this time 6-chloro-2-methoxyhydroquinone precipitated in the form of white needle crystals, with m.p. 140°. However, for the additional oxidation it is not necessary to separate the hydroquinone derivative. The viscous mixture can be immediately added to the oxidizing mixture of 40 g of sodium dichromate in 70 ml of 20% sulfuric acid, cooled to −5° for 2 hours. The temperature at this point should be strictly maintained as with the derivative of methoxyquinone.

The 6-chloro-2-methoxyquinone was precipitated in the form of fine light-orange crystals. After termination of the oxidation, the mixture was left to stand for 1-2 hours at −5°, the precipitate filtered off rapidly, washed with iced water and dried with calcium chloride. The weight of dry methoxychloroquinone was 4.28 g, i.e., 77% of the theoretical.

After crystallization from alcohol – light-orange crystals in the form of long, thin needles with m.p. 158-159°; readily soluble in alcohol, ether, chloroform, glacial acetic acid; poorly soluble in water.

0.1573, 0.1422 g substance: 0.1301, 0.1184 g AgCl. Found %: Cl 20.48, 20.75. $C_7H_5O_3Cl$. Calculated %: Cl 20.57. 0.1672, 0.1304 g substance: 0.2273, 0.1779 g AgI. Found %: OCH_3 17.95, 18.01. $C_6H_2O_2Cl(OCH_3)$. Calculated %: OCH_3 17.97.

III. 5-Chloro-2-methoxyquinone. 2-Chloro-4-hydroxy-5-methoxybenzaldehyde resulted from chlorination of acetylvanillin, followed by subsequent saponification of the acetoxy group [6]. 5-Chloro-2-methoxyquinone resulted from oxidation of 2-chloro-4-hydroxy-5-methoxybenzaldehyde, according to the method described for the methoxyquinone, with maintenance of the same conditions. The authors obtained 3.3 g of 5-chloro-2-methoxyquinone, i.e., 60% of the theoretical yield, from 6 g of 2-chloro-4-hydroxy-5-methoxybenzaldehyde.

After crystallization from alcohol - light yellow crystals in the form of platelets with m.p. 172-173°. Soluble in alcohol, ether, chloroform, acetone, benzene, glacial acetic acid to a lesser degree than the 6-isomer; poorly soluble in water.

0.1533, 0.1384 g substance: 0.1272, 0.1144 g AgCl. Found %: Cl 20.56, 20.67. $C_7H_5O_3Cl$. Calculated %: Cl 20.57. 0.1355, 0.1520 g substance: 0.1706, 0.2076 g AgI. Found %: (OCH_3) 18.10, 18.03. $C_6H_2O_2Cl(OCH_3)$. Calculated %: OCH_3 17.97.

SUMMARY

The synthesis of two new compounds, 6-chloro-2-methoxyquinone and 5-chloro-2-methoxyquinone, by treating the isomeric chloro-vanillins with hydrogen peroxide in alkaline solution, followed by oxidation of the resulting hydroquinone derivatives, has been described.

6-Chloro-2-methoxyquinone crystallizes in the form of thin, yellow needles, with m.p. 159°; 5-chloro-2-methoxyquinone crystallizes in the form of orange-yellow platelets, with m.p. 173°. 5-Chloro-2-methoxyquinone is soluble in organic solvents to a lesser extent than the 6-isomer.

It has been shown that upon methoxylating chloroquinone with methyl alcohol in the presence of zinc chloride, there occurs in addition to the direct introduction of the methoxyl group, a substitution of chlorine by a second methoxyl group, with the formation of 2,5-dimethoxyquinone which does not contain chlorine; therefore, direct methoxylation of chloroquinone cannot be used for the synthesis of chloromethoxyquinones.

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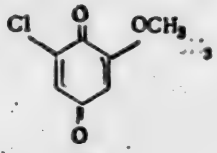
INVESTIGATIONS IN THE FIELD OF QUINONES

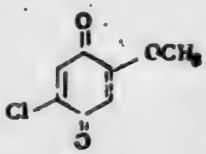
III. CHLORINATION OF METHOXYQUINONE

I. S. Ioffe and A. F. Sukhina

In the preceding article [1], derivation of 6-chloro-2-methoxyquinone (I) was described, as well as 5-chloro-2-methoxyquinone (II), starting with the isomeric chlorovanillins and unsuccessful attempts to synthesize chloromethoxyquinones by the methoxylation of chloroquinone.

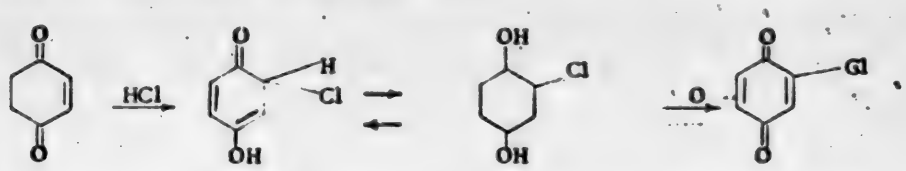


(I)



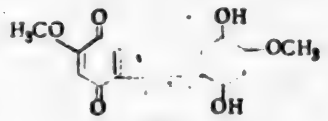
(II)

At the same time the authors studied the possibility of synthesizing these compounds by chlorination of methoxyquinone. The chlorination of quinones may be accomplished in two ways. One of them consists of treating quinone with anhydrous hydrogen chloride, followed by oxidation of the addition product which is tautomeric with the chlorohydroquinone, to form the corresponding chloroquinone. Thus, in particular, the monochloroquinone [2] is obtained from benzoquinone according to the scheme:

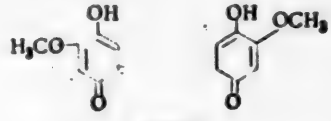


By the same procedure, a mixture of isomeric chlorotoluquinones [3] was obtained from toluquinone.

However, as investigations by the authors have shown, this method was found to be useless for synthesis of chloromethoxyquinones. Upon passing hydrogen chloride through a solution of the methoxyquinone in chloroform, a dark blue-violet precipitate separated which contained no chlorine, and after crystallization from nitrobenzene, melted at 238-240°. The same substance resulted upon addition of mineral acid to an acetate solution of methoxyquinone. It was found that this substance was identical with the already-described compound of the structure (IIIa) or (IIIb), obtained by oxidation of methoxyhydroquinone under specific conditions [4,5]:



(IIIa)



(IIIb)

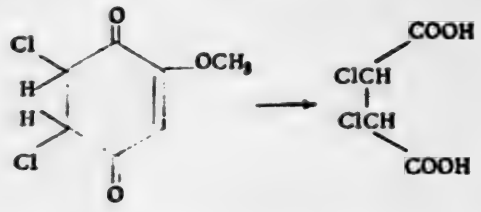
From the above-stated, it follows that methoxyquinone, in distinction to benzoquinone and toluquinone, is dimerized to a two-ringed compound under the influence of the methoxyl group in the presence of mineral acids, and that the interaction with hydrogen chloride cannot, therefore, be utilized for derivation of chloromethoxyhydroquinone, nor chloromethoxyquinone from methoxy quinone, respectively.

The second method for synthesis of monochloroquinones is based upon the interaction of quinone with chlorine. From the addition product resulting at the same time – quinonedichloride – the corresponding monochloroquinone can be obtained by splitting off hydrogen chloride. However, this method, as our experiments have indicated, is not applicable to all cases, and the possibility of its utilization depends upon the properties and the stability

of the resulting quinonedichloride. The simplest quinonedichloride, resulting from the addition of chlorine to benzoquinone, is very stable. It separates out in the form of colorless crystals, which melt sharply at 146° without decomposition. Nor does the colorless melt alter when heated to 160°. Only above 170-180° does the quinonedichloride slowly decompose with evolution of hydrogen chloride, but at this temperature the resulting monochloroquinone also breaks down. The toluquinonedichloride is somewhat less stable. It melts sharply at 135°, but the resulting melt at a temperature slightly higher than the melting point decomposes with the evolution of hydrogen chloride, and with formation of chlorotoluquinone. The methoxyquinonedichloride is even less stable. It begins to turn yellow above 100°, and at 120° melts with decomposition, evolving hydrogen chloride, with the formation of an orange melt, which, upon further heating, solidifies and again melts at 158-163°.

The above-indicated shows that the introduction of a methyl group, and to an even greater extent the methoxyl group, lowers the stability of the corresponding quinonedichlorides. It might be assumed that the quinonedichlorides resulting from interaction of chlorine with quinone derivatives would possess even less stability when containing several methyl or methoxyl groups. Indeed, when chlorine is passed through a solution of 2,6-dimethoxyquinone or 2,5-dimethylquinone in chloroform, under such conditions, when quinone, toluquinone or methoxyquinone is used, the corresponding dichlorides are obtained, 3-chloro-2,6-dimethoxyquinone [6] and 3-chloro-2,5-dimethylquinone [7] being obtained directly. It is possible under such conditions that the reaction proceeds by a preliminary addition of chlorine, with formation of the corresponding quinonedichlorides, but the latter are so unstable under the influence of 2-methyl or 2-methoxyl groups that they decompose with hydrogen chloride evolution, even at low temperature conditions of formation.

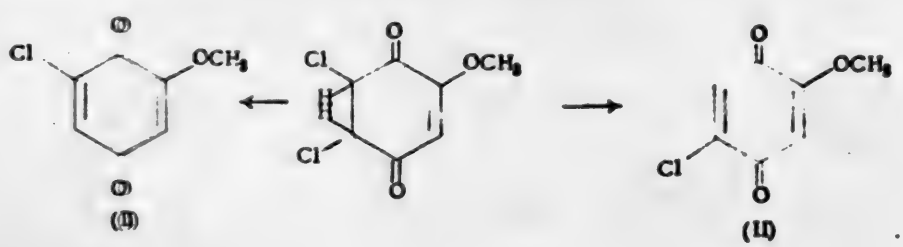
The comparatively low stability of methoxyquinonedichloride was utilized by the authors for a preparative synthesis of chloromethoxyquinones; at the same time, however, some unexpected results occurred. The methoxyquinonedichloride, itself, resulted [8] with comparative ease, on passing chlorine through a cooled solution of methoxyquinone in chloroform. Two chlorine atoms at the same time added to the double bond of that part of the quinone ring which was not connected with the methoxyl group. This was proved by the fact that upon oxidizing methoxyquinonedichloride, dichlorosuccinic acid resulted.



However, in the synthesis of methoxyquinonedichloride, there must be complete absence of even traces of hydrogen chloride in the chlorine which is passed through, which should be carefully checked, since the former promotes dimerization of the initial methoxyquinone into the above-indicated compound (III).

It was found that hydrogen chloride may also cause side reactions during the thermal decomposition of methoxyquinonedichloride; therefore, for the preparative synthesis of chloromethoxyquinone, the authors heated methoxyquinonedichloride under those conditions which promoted rapid elimination of hydrogen chloride from the reaction mixture. The authors placed a thin layer of methoxyquinonedichloride in a beaker, which was then placed in a thermostat heated to 125°. The product melted rapidly and solidified again in the form of a yellow-green crust. After cooling and powdering, the authors obtained a yellow powder which melted at 150-160°.

Decomposition of methoxyquinonedichloride, by splitting off hydrogen chloride, may lead to the formation of two isomeric chloromethoxyquinones:



Both of these chloromethoxyquinones were obtained by the authors [1] from the corresponding chlorovanillins. 6-Chloro-2-methoxyquinone crystallized out in the form of thin needles with m.p. 159°, and 5-chloro-2-methoxyquinone – in the form of platelets with m.p. 173°. The mixture of the two isomers begins to melt at approximately 130°.

The product obtained by the authors upon the thermal decomposition of methoxyquinonedichloride, melted sharply after crystallization from alcohol, at 173°. By analysis, by the properties, and by the mixing tests, it was identified with 5-chloro-2-methoxyquinone (II). The yield of this compound reached 70% of the theoretical. In the mother crystallization liquors the authors were unable to find the second isomer, 6-chloro-2-methoxyquinone (I). The absence of the latter is testified to by the fact that the crude, non-crystallized product of thermal decomposition of methoxyquinonedichloride melted at 160°, whereas a mixture of the two isomers begins to melt at a considerably lower temperature. The above-stated leads to the conclusion that the main product of thermal decomposition of methoxyquinonedichloride is 5-chloro-2-methoxyquinone.

Methoxyquinonedichloride is also unstable when heated in a number of solvents. The authors were convinced of this fact during attempts to crystallize the compound. Methoxyquinonedichloride solutions in alcohol in particular became yellow on heating and acquired an acid reaction as the result of hydrogen chloride evolution. The authors decided to use this observation for what seemed to be a more convenient preparative synthesis of chloromethoxyquinone. Indeed, upon introducing methoxyquinonedichloride into a boiling aqueous alcohol, with subsequent cooling of the solution, a yellow-colored crystalline precipitate separated out in a yield of about 60% of theoretical. However, this substance was found not to be 5-chloro-2-methoxyquinone. After crystallization, the resulting substance melted at 159°, and was identified with 6-chloro-2-methoxy-quinone (I).

Thus experiments have shown that upon decomposing methoxyquinonedichloride by splitting off hydrogen chloride, the direction of the reaction and the structure of the resulting chloromethoxyquinone depends upon the conditions of reaction. With thermal decomposition of methoxyquinonedichloride in the absence of solvent, the principal reaction product is found to be 5-chloro-2-methoxyquinone; upon heating with aqueous alcohol, the principal reaction product is found to be 6-chloro-2-methoxyquinone.

Further development of the work has demonstrated that the reaction direction also depends upon the character of the solvent. Thus, for example, upon introducing methoxyquinonedichloride into acetic acid heated to boiling, the solution immediately becomes yellow, and upon cooling, 5-chloro-2-methoxyquinone separates, which, after crystallization, melted at 172-173°. The same product will result when methoxyquinonedichloride is introduced into boiling anhydrous acetone. When methoxyquinonedichloride is introduced into 25% acetic acid heated to boiling, or into acetone diluted with water, 6-chloro-2-methoxyquinone results, m.p. 158-159°.

These experiments indicate that when methoxyquinonedichloride is heated in the absence of solvents, or in anhydrous solvents, hydrogen chloride cleavage proceeds in one specific direction, with the formation of 5-chloro-2-methoxyquinone; but upon heating in aqueous solvents, cleavage of hydrogen chloride proceeds in the other direction, with formation of 6-chloro-2-methoxyquinone. The same product will result when quinonedichloride is introduced into boiling water. Upon heating methoxyquinonedichloride in aromatic hydrocarbons, however, methoxyquinone is very stable. It does not decompose even upon one-hour boiling in xylene, which boils above the decomposition point of the crystalline methoxyquinonedichloride. By using benzene as the solvent, the authors were able to recrystallize methoxyquinonedichloride, thus obtaining it in the form of fine, almost colorless crystals, with decomposition point 120°. However, it was sufficient to add to the benzene only a few drops of water and the decomposition proceeded rapidly, with formation of 6-chloro-2-methoxyquinone.

SUMMARY

Upon passing hydrogen chloride through methoxyquinone solution in organic solvents, a dimerization product of methoxyquinone results immediately, precipitating in the form of a dark violet solid, melting at 238-240° after recrystallization from nitrobenzene, and is identical with that product described in the literature which is the oxidation product of methoxyhydroquinone. Therefore such a method cannot be used for the synthesis of chloromethoxyhydroquinone and, respectively, the chloromethoxyquinone by analogy with chlorohydroquinone.

For such purpose methoxyquinonedichloride can be used, which is obtained by passing chlorine through a solution of methoxyquinone in chloroform. In distinction to benzoquinonedichloride which boils sharply at 146°, and is stable to heat up to 160°, methoxyquinonedichloride when heated to 120° decomposes with evolution of hydrogen chloride and with conversion to 5-chloro-2-methoxyquinone.

Methoxyquinonedichloride is also unstable when heated in many organic solvents. Here the cleavage of hydrogen chloride, depending upon the character of the solvent, proceeds in two directions with the formation o two isomeric chloromethoxyquinones. Upon introducing methoxyquinonedichloride into anhydrous acetic acid o acetone, the same 5-chloro-2-methoxyquinone (m.p. 172-173°) is formed as that formed by melting crystals of methoxyquinonedichloride; however, in water, and also in aqueous acetic acid, acetone or alcohol, 6-chloro-2-methoxyquinone is formed (m.p. 159°).

Methoxyquinonedichloride is stable upon heating in benzene, toluene and xylene, and can be recrystallized from these solvents without decomposition.

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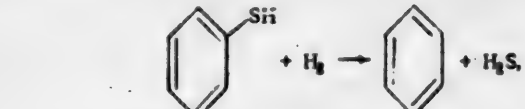
THE CATALYTIC TRANSFORMATION OF THIOPHENOL, DITHIORESORCINOL, THIANTHRENE AND DIPHENYLSULFIDE OVER ALUMINOSILICATE CATALYST

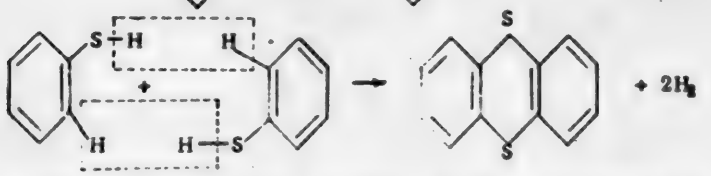
I. N. Tits-Skvortsova, A. I. Leonova, S. Ya. Levina and E. A. Karaseva

In the present work, data are given for the synthesis and catalytic transformation of sulfur compounds of the aromatic series, having as their composition divalent sulfur, namely: thiophenol, dithioresorcinol, thianthrene and diphenylsulfide. Synthesis of the aromatic sulfur compounds was carried out by procedures described in the literature. In some procedures slight modifications were introduced. To obtain comparative results, the investigated sulfur compounds were passed over aluminosilicate catalyst under standard conditions [1] adopted by the authors.

Thiophenol was taken as the simplest of the aromatic thiols, and was passed over aluminosilicate catalyst at 200°, 300° and 500°. In all of the experiments, benzene, thianthrene and the initial thiophenol were isolated from the catalyzate. The waste gases contained large amounts of hydrogen sulfide. Judging from the substances obtained, thiophenol on contact with catalyst undergoes transformation in two directions:



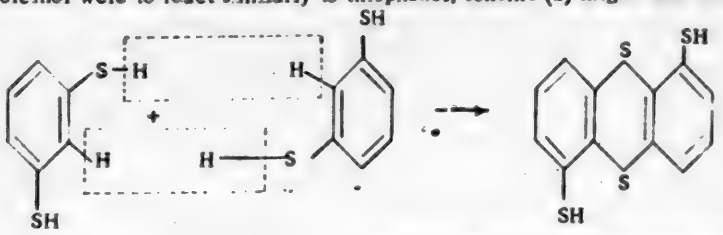
(1)



(2)

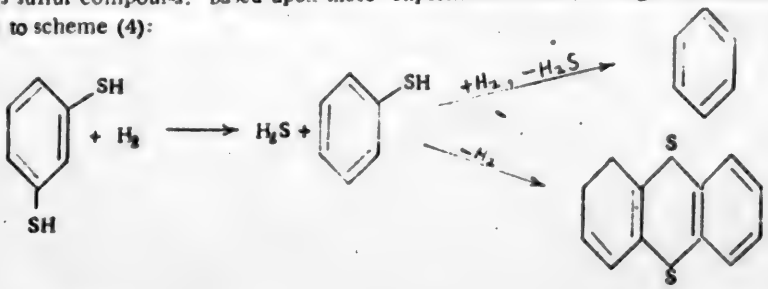
As the result of destructive hydrogenation, thiophenol is converted into benzene and hydrogen sulfide; dehydrogenation proceeds in a similar manner, leading to formation of two thiophenol molecules from the thianthrene molecule. Reaction (1) should be considered as the principal course of the reaction, since 4 times as much benzene is formed as thianthrene.

If dithioresorcinol were to react similarly to thiophenol, scheme (2) might take the following form:



(3)

It was of interest to clarify whether such a disulfhydryl derivative of thianthrene results from dithioresorcinol. The experiment with dithioresorcinol was carried out at 300°; benzene (23.8% of catalyzate weight) was separated from the resulting catalyzate, thiophenol (11.9%) and thianthrene (25.3%). About 50% of the sulfur that was contained in the initial dithioresorcinol was evolved in the form of hydrogen sulfide. The remaining sulfur was left in the catalyzate as sulfur compound. Based upon these experimental data, it might be assumed that the process proceeds according to scheme (4):

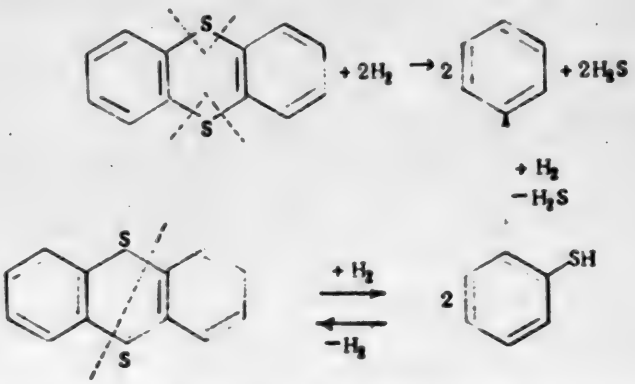


(4)

As the result of destructive hydrogenation, dithioresorcinol is converted into thiophenol. The latter, according to schemes (1 and 2) converts into benzene and thianthrene. Analysis of the waste gas after removal of hydrogen sulfide from it indicated the possibility of a hydrogenation reaction. The gas was composed chiefly of hydrogen and nitrogen. More complex compounds than thianthrene were not found in the catalysate; consequently, the reaction does not proceed according to scheme (3).

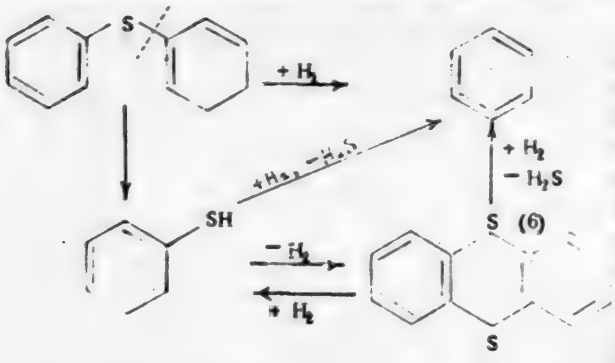
Since thianthrene was obtained from both thiophenol and from dithioresorcinol, it might be supposed that it is a stable compound. To verify this assumption, thianthrene was passed over aluminosilicate catalyst at 400°. Upon this it decomposed with evolution of hydrogen sulfide, but the decomposition was far from complete: unchanged thianthrene constituted about 45% of the catalyzate weight. The liquid portion of the catalyzate contained benzene (30% of the catalyzate weight) and traces of thiophenol.

The decomposition of thianthrene can be shown according to the following scheme:



The fundamental process appears to be the destructive hydrogenation of thianthrene, leading to evolution of sulfur in the form of hydrogen sulfide, and to benzene formation. The hydrogenation of thianthrene to thiophenol evidently proceeds only to a small extent; but since the process is reversible (scheme 2), and the resulting thiophenol is further reduced irreversibly to benzene (scheme 1), then it becomes clear why only traces of thiophenol are present in the catalyzate.

For a study of the catalytic transformation of aromatic sulfides, the simplest of them was synthesized – diphenylsulfide, which was passed over aluminosilicate catalyst at 300, 350, 450 and 500°. From the catalyzates obtained, only two products were separated in all of the cases – benzene and thianthrene. The yield of benzene increased with increase in temperature, but the quantity of thianthrene decreased with increase in temperature. The reason is clear from the preceding: thianthrene itself converts into benzene at higher temperature. The catalyzates contained only traces of thiophenol. Evolution of hydrogen sulfide was observed at all temperatures investigated. Transformations of diphenylsulfide upon contact with aluminosilicate may be expressed by scheme (6).



At first, as the result of a destructive hydrogenation, diphenylsulfide decomposes, forming benzene and thiophenol. Thiophenol then irreversibly converts into benzene, according to the preceding (schemes 1, 2, and 5), and reversibly into thianthrene. Thianthrene is found to be the most stable of all sulfur compounds studied, but it also partially converts to benzene (scheme 5). The presence of thianthrene in the catalyzates indicates that its rate of formation is higher than its rate of decomposition. For thiophenol the correlation is in reverse: the catalyzate contains only traces of it. As can be seen from scheme (6), the principal reaction in all of these transformations is found to be destructive hydrogenation, and all of the processes proceed irreversibly to the formation of aromatic hydrocarbon, with evolution of the sulfur in the form of hydrogen sulfide.

If the transformation observed upon contact of sulfur compounds of the aliphatic series with aluminosilicate are compared with the transformations of aromatic sulfur compounds, differences in these transformations should be noted. Whereas a variety of reactions [2] is observed with the aliphatic series (simple hydrogen sulfide evolution,

disproportionation of hydrogen, destructive hydrogenation), the main and most characteristic process in the aromatic series appears to be destructive hydrogenation, and the dehydrogenation reaction plays only a secondary role. The final products of transformation of sulfur compounds are also different: in the aliphatic series they are the alkenes, and in the aromatic series – the aromatic hydrocarbons. The common factor appears to be that the process in both the aliphatic and the aromatic series proceeds irreversibly toward the formation of hydrocarbons, and at the same time sulfur is evolved in the form of hydrogen sulfide.

EXPERIMENTAL

Sulfur compounds were passed over the catalyst under the following conditions: aluminosilicate catalyst in the amount of 30 g was placed in a reaction tube which was heated in an electric furnace. The experiment was carried out by a circulation method, passing the sulfur compounds over the catalyst in a weak stream of nitrogen (passage rate of the nitrogen was 600-800 ml per hour). The volumetric rate of flow of the substance was 0.25. In all cases of contact between the sulfur compounds and the catalyst, evolution of hydrogen sulfide was observed. The solid portion of catalyzate was filtered off and recrystallized from alcohol, the liquid portion washed with water until the hydrogen sulfide was removed, dried and fractionated to separate individual compounds from it. During fractionation there always resulted lower and higher fractions, which also indicated cracking and condensation reactions. Regeneration of catalyst was carried out after each experiment by letting in a stream of air at 500°, up to the point of whitening of the catalyst, the air being removed from the reaction tube by nitrogen.

Thiophenol. Obtained by reduction of benzenesulfonyl chloride by two methods: a) using zinc dust as the reducing agent, b) using tin and hydrochloric acid as the reducing agent. Benzenesulfonyl chloride was obtained from benzene and chlorosulfonic acid [3] in 70% yield. 156 g of pure thiophenol was obtained from 320 g of benzenesulfonyl chloride by reduction with zinc and sulfuric acid [4]. The yield was 78.3% of the theoretical. B.p. was 68° (22 mm); n_D^{20} 1.5890; d_4^{20} 1.0787. The method of reducing benzenesulfonyl chloride by the use of tin and hydrochloric acid takes less time, is easy to carry out, but gives a lower yield of thiophenol and is economically inconvenient. 28 g of thiophenol (55% of the theoretical yield) was obtained from 80 g of benzenesulfonyl chloride. B.p 50.5-51.5° (7 mm); n_D^{22} 1.5883, d_4^{22} 1.0735.

Literature data: b.p. 71° (15 mm [4]); b.p. 77° (30 mm); $n_D^{23.2}$ 1.5861; $d_4^{23.2}$ 1.0739 [C].

The resulting thiophenol was passed over aluminosilicate catalyst under standardized conditions at 200, 300 and 500°. In all cases the catalyst obtained was a mixture of liquid and solid substances. After their separation, the liquid portion was fractionated. The solid substance separated from the higher fractions was combined with the solid substance from the catalyzate, the crystals were pressed out on a porous plate and crystallized from alcohol. The individual compounds resulting from the catalyzate, and their constants, are given in Table 1.

TABLE 1

Catalysis of Thiophenol at 200, 300 and 500°

temperature	thiophenol taken (g)	catalyzate obtained (g)	substances separated from catalyzate	quantity (g)	% yield of catalyzate weight	temperature: boiling	temperature: melting	n_D^{20}
200°	21.6	11.7	benzene	5.8	49.5	80.5-81°*	–	1.5004
			thianthrene	1.3	11.1	–	155° **	–
			thiophenol	0.9	7.7	164-166	–	1.5862
300	21.6	10.65	benzene	4.5	42.2	80-84	–	1.5020
			thianthrene	1.7	15.9	–	155	–
			thiophenol	0.7	6.6	165-166	–	1.5860
500	21.6	13.0	benzene	4.3	33.0	80-83	–	1.5018
			thianthrene	1.65	12.7	–	154	–
			thiophenol	1.9	14.6	165-166	–	1.5880
500	13.5	7.9	benzene	2.4	30.4	79-80	–	1.5002
			thianthrene	0.8	10.1	–	151	–
			thiophenol	1.4	17.7	164-166	–	1.5882

* According to the literature data [7] b.p. = 80.1°; n_D^{20} 1.5012.

** According to the literature data [8]: m p = 154-158°.

As can be seen from the data of Table 1, the principal substance resulting from the passage of thiophenol over the catalyst was found to be benzene. Thianthrene resulted at 200-300°, approximately four times less in amount than benzene.

The catalyzate obtained at these temperatures contained a small quantity of thiophenol. The presence of a large quantity (14.6%) of initial thiophenol in the catalyzate obtained at 500° created some doubt as to the activity of the catalyst. The catalyst was therefore regenerated for 10 hours at 500°. As can be seen from the data of the Table, the repeated experiment, carried out at 500°, confirmed the results of the preceding experiment.

The presence of a large amount of initial thiophenol in the catalyzate obtained at 500° may be explained by the fact that at this temperature all of the thiophenol is removed from the catalytic tube, while at 200 and 300° a portion of the thiophenol is retained. The fluctuations in thianthrene yields, however, are explained by unavoidable losses during its crystallization.

The total thianthrene obtained from the thiophenol was once more recrystallized from alcohol. Its melting point did not change and remained equal to 155°. It gave a characteristic blue coloration with concentrated sulfuric acid. A determination of C, H and S by the M. O. Korsun [9] method gave the following results:

6.840 mg substance: 16.700 mg CO_2; 2.280 mg H_2O; 6.035 mg SO_4. 6.120 mg substance: 14.949 mg CO_2; 2.020 mg H_2O; 5.420 mg SO_4. Found %: C 66.63, 66.57; H 3.73, 3.69; S 29.45, 29.56. $C_{12}H_8S_2$. Calculated %: C 66.61; H 3.73; S 29.66.

Dithioresorcinol was obtained by the method of Bourgeois [10]. This method, like that of the method for thiophenol synthesis, consisted of reducing m-benzenedisulfonylchloride with zinc dust and hydrochloric acid. The m-benzenedisulfonylchloride required for the reaction was obtained by the action of chlorosulfonic acid on benzene at high temperature.

To obtain m-benzenedisulfonylchloride, it was produced from benzene purified from thiophene by shaking with concentrated sulfuric acid. Sulfonation of the benzene was carried out in a round-bottomed flask, equipped with dropping funnel, reflux condenser and mechanical stirrer. 1950 g (16.8 moles) of chlorosulfonic acid was placed in the flask and 195 g (2.5 moles) of pure benzene added dropwise, with stirring, at room temperature. Reaction proceeded with the evolution of heat. The reaction mixture was then heated for 2 hours on an oil bath at 150-160°. After that the mixture was cooled to room temperature and was cautiously poured into a container filled with ice, with stirring. Strong heat evolution was observed here, and provision should be taken that there is always enough ice. At the end of the addition a brown-colored precipitate formed on the bottom of the container. The precipitate was filtered off and dried in air. The weight of crude product was 485 g (70.8% of the theoretical yield). To purify, the benzenedisulfonyl chloride was twice recrystallized from gasoline freshly distilled (b.p. 85-150°). 200 g (0.73 mole) of m-benzenedisulfonyl chloride was obtained, which amounted to 29.2% of theory. Light-colored crystals with m.p. 61-61.5°.

Literature data: m.p. 63° [11].

The resulting m-benzenedisulfonyl chloride was reduced, without further purification, to thioresorcinol. For this purpose 180 g of zinc dust and 200 ml of water were placed in a round-bottomed, three-necked flask equipped with reflux condenser and mechanical stirrer. The mixture was heated to 50° on a water bath, and 75 g (0.27 mole) of the m-benzenedisulfonyl chloride was added with stirring through the third neck of the flask. 20 g more of zinc dust was then added and the mixture heated on a water bath for 10 minutes at 70°.

The flask contents were cooled to 20°, and this temperature was maintained until a precipitate formed on the bottom of the flask in the form of a paste, grayish in color. A dropping funnel was placed in the third neck of the flask, and 1 kilogram of hydrochloric acid (sp. gr. 1.18) diluted with 500 ml of water, was added slowly, with mixing. The reaction was violent, and the flask was cooled with water.

Another 25 g of zinc dust was added and stirred for 2 hours at 20°. A caked precipitate formed on the bottom of the flask, gray in color. The acid layer was poured off from the precipitate, the precipitate filtered off, transferred from the beaker and repeatedly extracted with ether until the ether extract gave a mercaptan reaction (doctor test). The filtrate resulting from filtration of the precipitate was extracted three times with ether. The ether extracts were combined and dried with magnesium sulfate. After distilling off the ether, the dithioresorcinol was twice distilled in vacuo. The yield was 29.5 g (77.7% of theoretical). B.p. 128-128.5° (16 mm); m.p. 26-26.5°.

Literature data: b.p. 132° (20 mm); m.p. 27° [10].

Catalytic Transformation of Dithioresorcinol. 29 g of dithioresorcinol was passed over freshly-regenerated aluminosilicate catalyst at 300° under standardized conditions. In order that it might be introduced into the oven in the liquid state, the dropping funnel was warmed gently. The reaction was accompanied by a copious evolution of hydrogen sulfide. The weight of resulting catalyzate (a mixture of the liquid and the solid substances) was 6.7 g, which constituted 23.1% of the weight of dithioresorcinol taken. The solid portion of the catalyzate was separated from the liquid. The liquid catalyzate was washed with water to remove hydrogen sulfide and repeatedly extracted with 20% aqueous solution of KOH to recover mercaptans from it. After removal of alkali by washing with water, and drying with calcium chloride, benzene was isolated from the catalyzate in the amount of 1.6 g (23.8% of the catalyzate weight), with a b.p. of 79-80° (754 mm); n_D^{20} 1.5000; d_4^{20} 0.8770.

The alkaline extractions containing mercaptan were decomposed with hydrochloric acid, the mercaptan extracted with ether, the ether extracts washed to remove acid, and dried with magnesium sulfate. After distilling off the ether, thiophenol resulted (0.8 g), 11.9% of the catalyzate weight. B.p. was 166-169° (754 mm); n_D^{20} 1.5870; d_4^{20} 1.0716.

Thianthrene in the amount of 1.7 g (25.3% of the catalyzate weight), with m.p. 155-156°, was separated from the solid phase of the catalyzate by pressing out on a porous plate and crystallizing from alcohol. A sample mixed with an analyzed sample preparation of thianthrene did not give depression.

Hydrogen sulfide evolving during the course of the reaction was trapped by plumbite. The weight of washed and dried PbS precipitate was 51 g, which corresponded to 7.25 g of hydrogen sulfide, or 6.83 g of sulfur (52.1% of the theoretically possible). The sulfur remaining in the catalyzate was in the form of sulfur compounds.

An analysis of the outgoing gases, from which hydrogen sulfide was removed, gave: CO_2 0.26%, O_2 1.8%, H_2 10.5%, no CO, 0.6% saturated, no unsaturated, the remaining – nitrogen. The presence of hydrogen and of gaseous hydrocarbons in the gases indicated a cracking reaction.

Catalytic Transformation of Thianthrene. 5 g of thianthrene with m.p. 155-156° was passed over freshly-regenerated aluminosilicate catalyst at 400°. For this purpose the thianthrene was placed in the cold portion of the catalyst tube which projected out from the furnace. Upon gradually pushing the tube into the furnace, the thianthrene melted and flowed into the tube. Evolution of hydrogen sulfide was observed. The weight of resulting catalyzate (a mixture of liquid and solid) was 1.1 g (22% of the thianthrene weight taken). 0.7 g of benzene with n_D^{20} 1.5090 was separated from the liquid portion of the catalyzate. After repeated distillation, the benzene weight was 0.4 g (36% of the catalyzate weight), n_D^{20} 1.5000; m.p. 4°.

After distilling off the benzene, there remained in the flask several drops of high-boiling liquid with the characteristic sharp odor of thiophenol and a crystalline substance which was pressed out and combined with the solid portion of catalyzate. The solid substance, when recrystallized from alcohol, weighed 0.5 g (45% of the catalyzate weight) and melted at 155°. This was the initial, unchanged thianthrene.

Diphenylsulfide. This was obtained by the action of sulfur monochloride on benzene in the presence of aluminum chloride [12]. 177 g (2.3 mole) of benzene purified to remove thiophene was placed in a round-bottomed flask equipped with mechanical stirrer, dropping funnel and a reflux condenser, along with 91 g (0.69 mole) of finely-ground commercial aluminum chloride. 85 g (0.6 mole) of sulfur monochloride in 81.5 g (1.04 mole) of benzene was added to the reaction mixture with stirring. The reaction mixture temperature was 10-13°. The aluminum chloride gradually disappeared and a dark-brown complex was formed. The reaction mixture was then stirred for an hour without cooling, and 1.5 hours at 30-40°, to the cessation of hydrogen chloride evolution. The resulting complex was decomposed with water and poured slowly, with stirring, into a container with ice chips. Decomposition proceeded violently, the color of the liquid changing from black to light yellow. A large quantity of sulfur deposited on the bottom and walls of the container. The liquid was transferred to a separatory funnel and the upper benzene layer was separated from the lower aqueous layer. The benzene layer was filtered off and the benzene distilled off. The remaining oil was cooled to 0°, again filtered to remove sulfur, and dissolved in methyl alcohol. The resulting solution was stirred for 3 hours at 0° and filtered off from the sulfur. After distilling off the alcohol, the diphenylsulfide was redistilled in vacuo at 147° (7 mm). To obtain a colorless preparation, the resulting diphenylsulfide was twice redistilled in vacuo. Yield was 86 g (76.6% of theoretical). B.p. 162.5° (18 mm); n_D^{20} 1.6312; d_4^{20} 1.1100.

Literature data: b.p. 162-163° (18 mm)[12]; $d^{15.8}$ 1.1175 [13]; $n_D^{18.5}$ 1.635 [14].

The diphenylsulfide obtained was passed over aluminosilicate catalyst under standard conditions at 300, 350, 450 and 500°. In all cases evolution of hydrogen sulfide was observed.

The liquid portion of the catalyzate was fractionated. The solid portion was pressed out on a porous plate and crystallized from alcohol.

The individual compounds separated from the catalyzate, and their constants, are given in Table 2.

TABLE 2

Catalysis of Diphenylsulfide at 300, 350, 450 and 500°

temperature	diphenylsulfide taken (g)	catalyzate obtained (g)	substances separated from catalyzate	quantity (g)	% yield of catalyzate wt.	temperature		n_D^{20}
						boiling	melting	
300°	11	9.7	benzene	0.7	8.0	78-80°	5-6°	1.5030
			thianthrene	1.2	13.7	–	153	–
			diphenylsulfide	4.8	55.2	150-155 (12 mm)	–	1.6364
350	11	5.4	benzene	1.6	29.6	79-80	5.2-6	1.5020
			thianthrene	0.8	14.8	–	152.6	–
			diphenylsulfide	traces	–	–	–	1.6327
450	11	5.1	benzene	1.8	35.3	79-81	–	1.5018
			thianthrene	0.75	14.7	–	154	–
500	11	6.2	benzene	4.0	64.5	78-80	–	1.5012
			thianthrene	0.7	11.3	–	152	–

As can be seen from the data of Table 2, the same substances, namely, benzene and thianthrene, result from the catalytic transformation of diphenylsulfide carried out over a wide range of temperatures. The yield of benzene increases with increased temperature, and the quantity of thianthrene decreases with increase in temperature. The initial diphenylsulfide was found in considerable quantity only at 300°. At all indicated temperatures, the strong, characteristic odor of thiophenol was evident.

SUMMARY

1. Sulfur compounds of the aromatic series undergo the following transformations upon contact with aluminosilicate catalyst at 300-500°:

a) thiophenol, as the result of destructive hydrogenation, converts into benzene and hydrogen sulfide: the process does not go to completion, simultaneously, but to a lesser degree, the dehydrogenation reaction proceeds with formation of thianthrene;

b) dithioresorcinol, as the result of destructive hydrogenation, converts at first into thiophenol, which then transforms as indicated above;

c) thianthrene, as the result of destructive hydrogenation, converts partially into benzene and hydrogen sulfide;

d) diphenylsulfide gives at first benzene and thiophenol, and the latter then transforms, according to point "a" above.

2. A destructive hydrogenation reaction is the principal, most characteristic reaction when sulfur compounds come in contact with aluminosilicate catalyst. The final transformation products are found to be aromatic hydrocarbons, the sulfur evolving as hydrogen sulfide. The decomposition process of sulfur compounds does not go to completion because of the high stability of some of them (thiophenol, thianthrene).

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INVESTIGATION IN THE FIELD OF HETEROCYCLIC COMPOUNDS

I. SYNTHESIS OF (QUINOLYL-6)-ALKANOLAMINES

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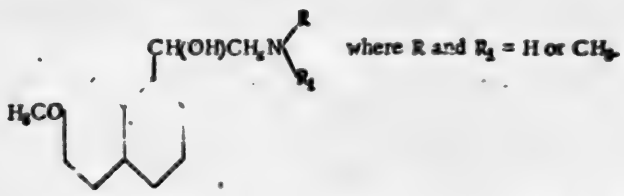
Aryl-β-aminoalkanols have been the objects of investigation for many years; the first stimulus to such work was the discovery of such interesting (in the pharmacological sense) natural compounds as adrenalin and ephedrine. The determinator of action of these compounds as pressor substances is conditioned by a characteristic side chain structure [1], having the character: $R_1CH(OH)\underset{R_2}{\underset{|}{C}}HNH_2$, where R_1 = an aromatic radical, R_2 = H or CH_3.

A great significance for the development of this work within the past few years is in connection with a concept expressed by Kaufman [2] back in 1913, to the effect that quinine in its structure may be considered to be an adrenalin-like substance, being a characteristic form of substituted aminoalkanol in the quinoline series, namely 4-(α-hydroxy-β-dialkylaminoalkyl)-6-methoxyquinoline. Proceeding from these premises, Kaufman [2] synthesized for the first time the simplest compound of this type, namely 4-(α-hydroxy-β-dialkylaminoethane)-6-methoxyquinoline:



It is of interest to note that this synthetic substance, constructed on the order of natural α-substituted amino alkanols, possesses a pressor action similar to them. In order to more closely approximate the structure of these substituted β-aminoethanols to that of quinine, Kaufman and his co-workers [3] further synthesized a number of α-substituted β-aminoethanols, differing only in the nature of the β-substituted radicals on the nitrogen side chain. Recently, in connection with the development of an enormous amount of investigation directed toward the search for new antimalarial preparations, the aminoethanols of the quinoline series again attracted the attention of many chemists. From this viewpoint the works of Campbell and his group of co-workers [4,5] deserves mention. A majority of these investigations is devoted to synthesis of α-substituted β-aminoalkanols contained as the side chain in the 4- or 8 position of the quinoline ring. The exception is one work of the authors, who, on the assumption that 2-and 4-substituted quinolines are chemically similar, considered it worthwhile, for pharmacological research, to synthesize a derivative containing the alkanolamine side chain in the 2-position of the quinoline ring. The direction of these works is evidently conditioned first of all by the fact that up to the present time all of the known antimalarial preparations of the quinoline series—both natural and synthetic—are found to be 4- or 8-substituted quinolines. Furthermore, there are absolutely no works on such synthesis, so far as the authors are aware, of those substituted aminoalkanols in which the side chain is present in any other position (apart from the 8) of the benzene ring of the quinoline molecule. Synthesis of such a series of compounds undoubtedly offers considerable interest. The fact that the above-indicated α-(4-quinolyl)-β-aminoethanols of Kaufman (cited above), clearly possess vasoconstrictive action can be considered as an interesting case which confirms the position expressed by Barger [1] to the effect that in the character of this side chain is to be found one of the decisive factors determining manifestation of pressor action. But there are no data on the extent to which the position of this side chain in the quinoline ring influences the physiological action, inasmuch as no compounds of such type have been synthesized.

The present work, which is part of a designed, systematic research, has for its purpose the filling of this gap, and is devoted to the synthesis of related new derivatives of the quinoline series, namely: (6-quinolyl)-

* Deceased.

β-aminoethanol and (6-quinolyl)-β-aminopropanol, of the general formula: $RCH(OH)CHNH_2$ (with R_1 on the CH) where R = the quinoline ring, R_1 = H or CH_3, $CH(OH)CHNH_2$ = side chain in position 6.

As the starting substance, the authors have taken 6-quinolylaldehyde, which has become a relatively accessible substance because of the work of M. A. Berkengeim and V. M. Rodionov [6]. By condensing it with the corresponding nitroalkanols in the presence of organic bases [7], the authors planned to obtain the substituted nitroalkanols, and by reduction (selective reduction of the nitro group) – the corresponding β-aminoalkanols. The authors carried out condensation of 6-quinolylaldehyde with nitromethane and nitroethane; condensation was carried out in alcoholic solution at ordinary temperature in the presence of diethylamine. The reaction proceeded very smoothly: by 24 hours the precipitation of well-formed slightly yellow crystals was observed, the quantity of which reached a maximum (about 80%) after 2-3 days. It is interesting to mention that the only reaction products were found to be the nitroalkanols, and in no case was it possible to determine the formation of unsaturated compounds.

Thus, in a respect, quinolylaldehyde parallels the properties of cinchonine aldehyde which, as was shown by Phillips [8], reacts with nitroalkane in an aldol-type condensation.

The second stage proceeds in a more complex manner, namely the synthesis of aminoalkanols. Although it was at once possible in the first orientation experiments to determine that reduction of the nitro group by hydrogen in the presence of Raney nickel catalyst proceeds quantitatively and selectively, judging from the quantity of hydrogen consumed, the yield of aminoethanols isolated in the form of hydrochloride salts was very low; and, moreover, it depended upon the amount of water in the medium in which reduction was carried out, fluctuating over a very wide range (27-73%). It was natural to assume that during the reprocessing of the reaction mixtures, the amino ethanols obtained by the authors, as with other compounds of this series, undergo hydraminic cleavage, transforming into quinoly ketone, which was also present in the yield of substances sought for. In fact, upon a careful investigation of the filtrate remaining after isolation of the hydrochloride salt of one of the aminoalkanols synthesized by the authors, it was possible to isolate a compound containing a functional ketone group, which readily gave a semicarbazone, and as analysis of the latter indicated was found to be none other than ethylquinolyl ketone. The formation of this compound may be indicated by the following scheme:

$$RC(OH)CHCH_3 \longrightarrow RC(OH)=CHCH_3 \longrightarrow RCOCH_2CH_3$$
(H, NH_2)

where R = the quinoline ring.

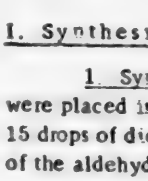
The authors further determined that this secondary ketone formation reaction is to a considerable degree dependent upon the amount of water in the alcohol in which reaction is carried out. The less water contained in the alcohol, the lower the ketone yield and the higher the aminoalkanol yield; fluctuating yields of the latter are therefore explained by this fact.

The resulting aminoalkanols were separated and characterized in the form of their hydrochloride salts.

EXPERIMENTAL

I. Synthesis of β-Nitroalkanols.

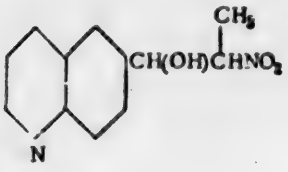
1. Synthesis of α (quinolyl 6) β-nitroethanol. 2.5 g of 6-quinolylaldehyde*, 30 ml of absolute ethyl alcohol were placed in a conical flask, and to the resulting suspension was added 3 ml of freshly-distilled nitromethane, and 15 drops of diethylamine, freshly distilled, was also added. Immediately upon introduction of the diethylamine all of the aldehyde dissolved, and the reaction mixture became slightly yellow. The flask was firmly stoppered with a cork and left to stand in a dark place at ordinary temperature for 48 hours. After 24 hours there appeared on the bottom of the flask a small quantity of cream-colored, well-formed, small crystals of the condensation product, and after 48 hours there was formed a copious, dense, cream-colored crystalline precipitate. It was filtered by suction and washed with a small quantity of cold alcohol; 2.15 g of substance resulted, constituting 67% of the theoretical yield; m.p. 137-138° (uncrystallized). After concentration of the filtrate and of the wash alcohol, it was possible to obtain a small quantity of crystals, but less pure. The resulting substance was readily soluble in hot alcohol, with greater difficulty in cold alcohol, and could be purified by crystallization from hot alcohol. A light, crystalline powder resulted, light-yellow in color, m.p. 139-140°.



* Obtained from 6-methylquinoline by its oxidation with selenium dioxide according to the method of M.A. Berkengeim and V. M. Rodionov (cited above).

0.09850 g substance: 0.2185 g CO_2; 0.0407 g H_2O. 0.1004 g substance: 0.2224 g CO_2; 0.0425 g H_2O. 0.0987 g substance: 10 ml N_2 (18°, 758 mm). 0.0858 g substance: 9.95 ml N_2 (22°, 762 mm). Found %: C 60.40, 60.40; H 4.67, 4.70; N 12.92, 12.85. $C_{11}H_{10}O_3N_2$. Calculated %: C 60.55; H 4.58; N 12.84.

The substance dissolved readily in acids, forming salts. The hydrochloride salt was obtained for characterization. For this purpose, 1 g of pure nitroalkanol (m.p. 139-140°) was dissolved in 30 ml of alcohol, 2 ml of 1% alcoholic hydrogen chloride solution was added, and having added absolute ether to a dilute suspension of the reaction mixture, was left to stand for several hours. The crystals (needles) which precipitated out, consisting of the hydrochloride salt, were recrystallized from hot alcohol; the yield of pure product was 56%. The salt was readily soluble in water, forming a slightly yellow solution; it did not melt at 250°; it began to decompose upon heating above 250°.



0.1082 g substance: 4.27 ml 0.1 N $AgNO_3$. Found %: Cl 13.99 (Folgard). $C_{11}H_{10}O_3N_2 \cdot HCl$. Calculated %: Cl 13.80.

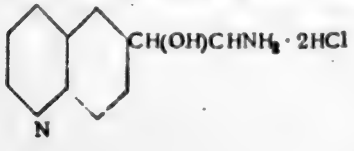
2. Synthesis of α-(quinolyl-6)-β-nitropropanol. 6-Quinolylaldehyde was condensed with nitroethane to obtain the derivative. 2.5 g of 6-quinolylaldehyde and 8 ml of absolute alcohol were introduced into a small conical flask; to the resulting suspension, 3.6 ml of freshly-distilled nitroethane and 15 drops of diethylamine also freshly distilled were added: complete dissolution of the aldehyde then occurred. The flask was stoppered firmly with a cork and left to stand at room temperature for 2 days. After this lapse of time, the precipitate was filtered by suction and washed with absolute alcohol. The alcohol was completely distilled off in vacuo from the filtrate. The precipitate, with the aid of a small quantity of alcohol, was transferred to the filter, filtered with suction, and washed with absolute alcohol. The combined precipitates were recrystallized from hot benzene. The total yield was 2.8 g, which constituted 77% of the theoretical yield: m.p. was 134°.

0.1234 g substance: 0.2802 g CO_2; 0.0580 g H_2O. 0.0976 g substance: 10.2 ml N_2 (23°, 758 mm). 0.1082 g substance: 12.0 ml N_2 (24.5°, 745 mm). Found %: C 61.97; H 5.22; N 12.02, 12.09. $C_{12}H_{12}O_3N_2$. Calculated %: C 62.07; H 5.17; N 12.07.

II. Synthesis of α-(Quinolyl-6)-β-aminoalkanols.

1. Synthesis of the Dihydrochloride of α-(quinolyl-6)-β-aminoethanol. 1 g of the above-obtained α-(quinolyl-6)-β-nitroethanol was dissolved with heating in 40 ml of absolute ethyl alcohol; the solution was transferred to a flask, stoppered firmly with a stopper equipped with two tubes; one was connected with a source of hydrogen, the other to a water pump. 5-10 g of Raney nickel catalyst was placed in the reaction flask, the former of which had been pre-washed with absolute alcohol to remove the water under which it is usually stored. Having removed all air from the apparatus as completely as possible with the aid of a water pump, the reaction flask was connected to a hydrogen source. Reduction was carried out under normal pressure and at standard temperature, with vigorous shaking of the reaction vessel, and reaction was terminated after 40 minutes, at which time the quantity of hydrogen calculated for reduction of the nitro group had been consumed, and the reaction mixture had become strongly alkaline. After termination of the reduction, the reaction mixture was filtered off from the catalyst; the latter was washed thoroughly with alcohol to the disappearance of alkaline reaction. The combined alcoholic filtrates were acidified with an alcoholic solution of hydrogen chloride and evaporated to dryness in vacuo. After distilling off the alcohol, a crystalline mass, yellow-brown or gray-green in color, remained (depending upon the standing time of the reaction mixture). After adding a few ml of absolute alcohol, the precipitate was transferred to a small Buchner funnel, carefully filtered by suction, washed with a small quantity of absolute alcohol and recrystallized from alcohol; the yield of crude product was 70-75%. yield of pure product was 35-40%.

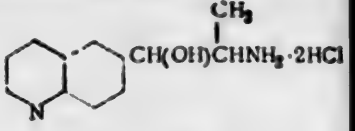
The dihydrochloride was recrystallized from alcohol as a fine, crystalline powder, readily soluble in water; it did not melt up to 250°, above which temperature it became black and decomposed.



0.1125 g substance: 0.2082 g CO_2; 0.0540 g H_2O. 0.1056 g substance: 9.75 ml N_2 (24°, 760 mm). 0.03740 g substance: 2.85 ml 0.1 N. $AgNO_3$. Found %: C 50.45; H 5.33; N 10.67; Cl 27.12 (Folgard); $C_{11}H_{12}ON_2 \cdot 2HCl$. Calculated %: C 50.60; H 5.36; N 10.73; Cl 27.18.

2. Synthesis of the dihydrochloride of α-(quinolyl-6)-β-aminopropanol. Reduction of the above-described α-(quinolyl-6)-β-nitropropanol, as well as treatment of the reaction mixture, was carried out under the same conditions as indicated above for its lower homolog. After distilling off the ether, a yellowish-brown mass remained, which crystallized out as a grayish-green, crystalline precipitate upon standing. To separate the dihydrochloride, after distilling off the alcohol, several ml of absolute alcohol was added to the residue, the precipitate transferred to a small Büchner funnel and thoroughly washed with a small quantity of absolute alcohol. The yield of uncrystallized product fluctuated within a wide range (from 23-25% in the case of high-colored residues after distilling off the ether, to 60-63%, in the case of gray.) To explain these fluctuations, both the crystalline reaction product and the filtrate remaining after isolation were investigated.

a) For an investigation of the precipitate it was carefully crystallized from alcohol; in this manner white crystals resulted (needles), readily soluble in water, and insoluble in the usual organic solvents (with the exception of hot alcohol). As analysis indicated, these crystals were the dihydrochloride of α-(quinolyl-6)-β-aminopropanol.



0.1244 g substance.: 0.2385 g CO_2. 0.0654 g H_2O. 0.1178 g substance: 10.25 ml N_2 (19°, 758 mm). 0.0586 g substance: 4.1 ml 0.1 N $AgNO_3$; Found %: C 52.29; H 5.84; N 10.13. Cl 25.62. $C_{12}H_{14}ON_2 \cdot 2HCl$. Calculated %: C 52.38; H 5.82; N 10.18; Cl 25.74.

b) An investigation of the filtrate was carried out by means of its extraction several times with ether; for this purpose the filtrate was saturated first with sodium acetate, after which an oil separated, which was extracted with ether. The ether extract was dried with freshly-heated sodium sulfate, and the ether distilled off; after distilling off the ether, the residue was dissolved in alcohol and treated with the corresponding quantity of a semicarbazide hydrochloride and sodium acetate, and left to stand overnight. The precipitate separated on the second day, was filtered off, and recrystallized from alcohol. White crystals with a yellowish shade, m.p. 218-220° As analysis showed, the crystals obtained were found to be the semicarbazone of α-(quinolyl-6)-β-ethyl ketone.

3.105 g substance: 0.657 ml N_2 (24°, 724.5 mm). 3.215 g substance: 0.684 ml N_2 (25°, 723.5 mm). Found %: N 23.19, 23.10. $C_{13}H_{14}ON_4$. Calculated %: N 23.14.

SUMMARY

1. The condensation reaction of 6 quinolyladehyde with nitroalkanes has been studied. It has been established that condensation proceeds according to the aldol type, with formation of the corresponding nitroalkanols.

2. The catalytic reduction reaction of α-(quinolyl-6)-β-nitroalkanols in the presence of Raney nickel has been studied. It has been determined that at normal pressure and atmosphere the reduction proceeds selectively, affecting only the nitro group, with formation of the corresponding β-aminoalkanols. It has been determined that while treating the reaction mixtures obtained after reduction, the β-aminoalkanols formed undergo hydramine cleavage, transforming into the corresponding ketones, identified as the semicarbazones.

3. Two new α-substituted β-aminoalkanols have been synthesized: α-(quinolyl-6)-β-aminoethanol and α-(quinolyl-6)-β-aminopropanol.

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SYNTHESIS OF 3-ALKYLCHOLESTADIENES

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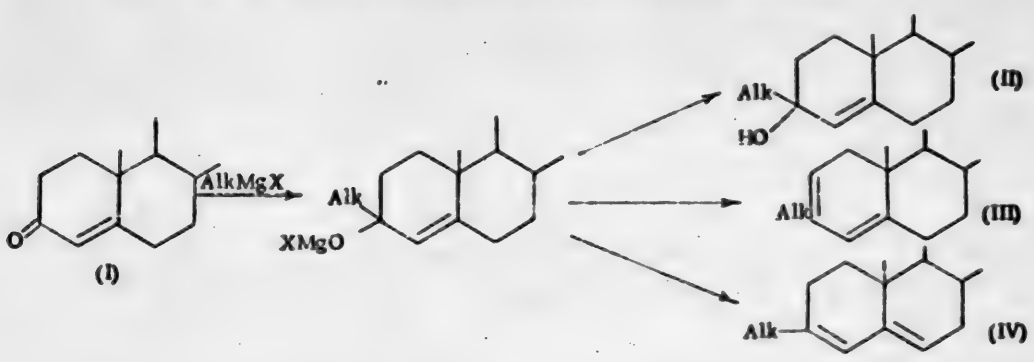
In spite of the considerable number of presently known dienes of the cholesterol series, of the substituted cholestadienes only two compounds are known – 3-chloro-$\Delta^{3,5}$-cholestadiene [1] and 3-phenyl-$\Delta^{3,5}$-cholestadiene [2]. The first was obtained by treatment of cholestenone with thionyl chloride, and the second, by interaction of cholestenone with phenylmagnesiumbromide, followed by decomposition of the Grignard complex with dilute hydrochloric acid.

Since cholestadienes with substituents in position 3 were of interest to the authors from the view of investigation of their photochemical transformations [3], the authors have used the latter method for the synthesis of various 3-alkylcholestadienes. The authors have investigated both conditions for the course of the Grignard reaction between cholestenone (I) and the various alkylmagnesium halides, the method of decomposing the resulting Grignard complex. All possible directions for this reaction can be shown by the following scheme:



As the authors' investigations have shown, the best conditions for reaction are found to be the addition, in ether solution, of a deficit amount of cholestenone (I) to the corresponding Grignard reagent with cooling and stirring. Depending upon conditions for the decomposition of the resulting Grignard complex, the authors were able to obtain both 3-alkyl-Δ^4-cholesten-3-ols (II) and various 3-alkyl-$\Delta^{3,4}$-cholestadienes (III), as well as 3-alkyl-$\Delta^{3,5}$-cholestadienes (IV).

Upon decomposing the Grignard complex with dilute hydrochloric acid, or acetic acid, there resulted as the principal product 3-alkyl-$\Delta^{3,5}$-cholestadienes (IV). The authors thus obtained 3-methyl-, 3-ethyl-, 3-n-butyl-, 3-cyclohexyl- and 3-hexyl-$\Delta^{3,5}$-cholestadienes.

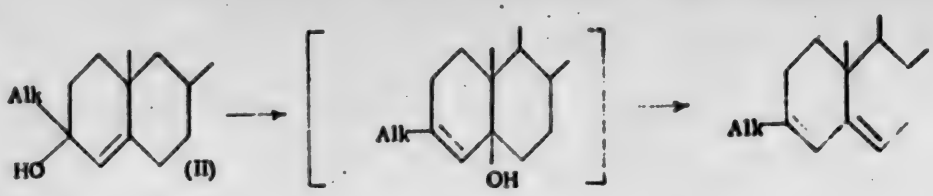
All of these dienes exhibit a strong rotation to the left, do not give normal addition products with maleic anhydride, are not reduced by sodium in amyl alcohol, and possess a maximum absorption below 250 mμ. All of these properties confirm the structure as 3-alkyl-$\Delta^{3,5}$ cholestadienes [4].

A summary of the 3-alkyl substitutes of $\Delta^{4,5}$-cholestadiene, and their physical properties, is given in the Table.

name	melting point	$[\alpha]_D$	yield (%)
3-methyl-$\Delta^{3,5}$-cholestadiene	81.5-82°	−129°	73.7
3-ethyl-$\Delta^{3,5}$-cholestadiene	77-78	−120	68.0
3-n-butyl-$\Delta^{3,5}$-cholestadiene	64-65	−109.9	51.8
3-hexyl-$\Delta^{3,5}$-cholestadiene	46-48	− 93.8	40.0
3-cyclohexyl-$\Delta^{3,5}$-cholestadiene	144-146	− 84.6	50.0

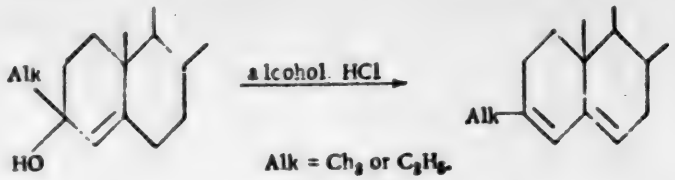
The direct formation of 3-alkyl-$\Delta^{3,5}$-cholestadienes under the conditions of acid decomposition of the Grignard complex may be explained by the possibility of ease in allyl rearrangement of the 3-alkyl-Δ^4-cholesten-3-ol (II) which first forms, with its subsequent dehydration according to the scheme:

* Deceased



The presence of such rearrangement identical with transformation of the allo- and epiallo-cholesterins [5] was experimentally confirmed by the authors.

If decomposition of the Grignard complex which results from the interaction of cholestenone with the alkylmagnesium halide is carried out under very mild conditions, with the calculated quantity of ammonium chloride, strong cooling and stirring, then in the case of CH_3MgI and C_2H_5MgBr it is possible to obtain from the reaction products 3-methyl-Δ^4-cholesten-3-ol (II, Alk = CH_3) and 3-ethyl-Δ^4-cholesten-3-ol (II Alk = C_2H_5) in yield up to 80%, together with some quantity of uncrystallizable substance. The 3-alkyl-Δ^4-cholesten-3-ols thus obtained are found to be readily crystallizable individual substances possessing a strong rotation to the right, which corresponds to a double bond position at C_4 [4]. Such carbinols are found to be extremely unstable compounds, as the result of which their isolation and crystallization require the maintenance of a series of precautions (see Experimental). Upon treating alcoholic solutions of the carbinols with hydrogen chloride in the cold, they are quantitatively decomposed to the corresponding 3-alkyl $\Delta^{3,5}$-cholestadienes which are identical with those resulting from direct acid decomposition:



This fact, which confirms the existence of allyl rearrangement in 3-alkyl-Δ^4-cholesten-3-ols, explains the direct formation of 3-alkyl-$\Delta^{3,5}$-cholestadienes by the direct acid decomposition of the interaction products of cholestenone with AlkMgX.

The authors were able to effect synthesis of 3-alkyl $\Delta^{3,4}$-cholestadienes only in the case of the methyl derivative. If the interaction product of cholestenone with CH_3MgI was decomposed under specified conditions (NH_4Cl solution without cooling), it was then possible to isolate a crystalline substance with m.p. 68-69°, $[\alpha]_D$ −12.8°, which by analysis, corresponded to 3-methylcholestadiene. This diene differed in its constants from the earlier obtained 3-methyl-$\Delta^{3,5}$-cholestadiene, and possessed an absorption in the range 260-280 mμ. When treated in alcoholic solution with hydrogen chloride, 3-methyl-$\Delta^{3,5}$-cholestadiene was formed in quantitative yield. These properties indicated that the 3-methylcholestadiene obtained, with m.p. 68-69°, and $[\alpha]_D$ −12.8° is 3-methyl-$\Delta^{3,4}$-cholestadiene (III Alk = CH_3).

An attempt to synthesize 3-methyl-$\Delta^{3,4}$-cholestadiene by direct dehydration of pure 3-methyl-Δ^4-cholesten-3-ol (sublimed in vacuo, redistilled with Al_2O_3 and so forth) did not lead to the desired results, since 3-methyl-$\Delta^{3,5}$-cholestadiene invariably resulted.

EXPERIMENTAL

I. Synthesis of 3-Alkyl $\Delta^{3,5}$-Cholestadienes.

1. Synthesis of 3-methyl-$\Delta^{3,5}$-cholestadiene. 5.7 g of cholestenone solution in 36 ml of absolute ether was added dropwise over a period of 0.5 hour, with vigorous stirring, and at a temperature of −8°, to a solution of methylmagnesium iodide, prepared from 1.4 g of magnesium and 9.2 g of methyl iodide in 50 ml of absolute ether (5-fold excess). After addition of the cholestenone, the reaction mixture was stirred for 1 hour at 0°, and then slowly decomposed by the addition of 50 ml of 10% HCl, with stirring and ice cooling. The ether extract was separated, washed thoroughly with water, and dried with anhydrous sodium sulfate. After distilling the ether off in vacuo, a light yellow oil remained, which crystallized after the addition of a small quantity of alcohol. After recrystallizing three times from a mixture of alcohol and ether (2:1), 4.2 g of pure 3-methyl-$\Delta^{3,5}$-cholestadiene was obtained. White, lustrous needles with m.p. 81-82° and $[\alpha]_D^{16}$ −129° (144 mg of substance in 10 ml of CCl_4, α 1.87°). The yield was 73.7%, calculating on the basis of cholestenone taken for reaction. For analysis, the product was dried in vacuo at 40° over phosphoric anhydride.

6.085 mg substance: 19.669 mg CO_2; 6.638 mg H_2O. 0.1232 g substance: 0.3975 g CO_2; 0.1328 g H_2O. Found %: C 88.21, 87.99; H 12.21, 11.97. $C_{28}H_{48}$. Calculated %: C 87.88; H 12.12.

3-Methyl-$\Delta^{3,5}$-cholestadiene does not give an addition reaction with maleic anhydride, nor is it reduced by sodium in amyl alcohol.

2. Synthesis of 3-Ethyl-$\Delta^{3,5}$-cholestadiene. 5.7 g of cholestenone in 36 ml of absolute ether was added to a four-fold excess of ethylmagnesium iodide solution (from 1.4 g of Mg and 7 g of C_2H_5I in 40 ml of absolute ether) over a period of 0.5 hour, with vigorous stirring and cooling to −8°. The reaction mass was then stirred for 1 hour at 0° and decomposed with 50 ml of a 10% solution of HCl. The ether extract was separated, washed thoroughly with water, and dried over anhydrous sodium sulfate. After distilling off the ether in vacuo, a light-yellow oil remained, which crystallized upon addition of a small quantity of alcohol. After recrystallizing 3 times from an alcohol-ether mixture (2:1), there resulted 4.0 g (68%) of 3-ethyl-$\Delta^{3,5}$-cholestadiene. Colorless, lustrous plates, with m.p. 77-78° and $[\alpha]_D^{15}$ −120.0° (100 mg of substance in 10 ml of CCl_4; α −1.2°). For analysis, the substance was dried in vacuo at 40° over phosphoric anhydride for 4 hours.

5.502 mg substance: 17.720 mg CO_2; 5.971 mg H_2O. 4.073 mg substance: 13.148 mg CO_2; 4.459 mg H_2O. Found %: C 87.89, 88.09; H 12.14, 12.25. $C_{29}H_{48}$. Calculated %: C 87.80; H 12.20.

3. Synthesis of 3-n-Butyl-$\Delta^{3,5}$-cholestadiene. A double excess of butylmagnesium bromide (from 0.6 g of Mg and 3.6 g of n-butyl bromide in 40 ml of absolute ether) was added to a solution of 5 g of cholestenone in 35 ml of absolute ether over a period of 40 minutes with vigorous stirring and ice cooling. After completion of the addition, the reaction mixture was kept at 0° for 1 hour, and then decomposed by adding a solution of 10 g of ammonium chloride in 80 ml of water, with vigorous stirring at 0°. The ether layer was separated, washed with water, and dried with anhydrous sodium sulfate. After distilling the ether off in vacuo, a thick, light-colored oil remained. The product was dissolved in 20 ml of warm ethyl alcohol and 0.5 ml of conc. HCl was added, with the result that a light-colored oil immediately separated out from the warm solution, which gradually crystalized upon standing in the refrigerator (for 2-3 days). The crystalline product was filtered off, washed with alcohol, and dried in a vacuum desiccator over calcium chloride. After recrystallizing twice from alcohol and ether mixture (3:1), there resulted 3.0 g of 3-n-butyl-$\Delta^{3,5}$-cholestadiene, with m.p. 64-65°, and $[\alpha]_D^{14}$ −109.9° (233 mg substance in 10 mg CCl_4, α −2.6°). The yield constituted 51.8%, based upon cholestenone taken for reaction.

For analysis, the 3-n-butyl-$\Delta^{3,5}$-cholestadiene was dried in a vacuum desiccator over phosphoric anhydride.

3.674 mg substance: 11.842 mg CO_2; 4.059 mg H_2O. 0.0801 g substance: 0.2584 g CO_2; 0.0888 g H_2O. Found %: C 87.95, 87.97; H 12.46, 12.32. $C_{31}H_{52}$. Calculated %: C 87.66; H 12.34.

4. Synthesis of 3-n-Hexyl-$\Delta^{3,5}$-cholestadiene. A double excess of hexylmagnesium bromide (from 0.63 g of Mg and 4.3 g of n-hexyl bromide in 35 ml of absolute ether) was added to a solution of 5 g of cholestenone in 35 ml of absolute ether, with vigorous stirring at 0°. After stirring for 1 hour at 0°, the reaction mixture was decomposed as before with ammonium chloride solution. The ether layer was separated, washed with water, dried over anhydrous sodium sulfate, and the ether distilled off in vacuo. The remaining viscous, colorless oil, which did not crystallize on standing, was dissolved in 30 ml of ethyl alcohol and 0.5 ml of concentrated HCl was added. The colorless oil which then separated out gradually crystallized upon prolonged standing in the refrigerator (10-12 days). The crystalline product was filtered off, washed with alcohol, and dried in a vacuum desiccator over calcium chloride. After double recrystallization from a small quantity of ethyl acetate, 2.3 g of pure 2-n-hexyl-$\Delta^{3,5}$-cholestadiene resulted with a constant m.p. of 46-48° and $[\alpha]_D^{15}$ −90.8° (252 mg substance in 10 ml CCl_4; α −2.5°). The yield was 40%, based on cholestenone.

For analysis, the diene was dried in a vacuum desiccator over phosphoric anhydride.

0.1042 g substance: 0.3344 g CO_2; 0.1202 g H_2O. 0.1026 g substance: 0.3288 g CO_2; 0.1160 g H_2O. Found %: C 87.52, 87.40; H 12.78, 12.56. $C_{33}H_{56}$. Calculated %: C 87.54; H 12.46.

5. Synthesis of 3-Cyclohexyl-$\Delta^{3,5}$-cholestadiene. A solution of 5 g of cholestenone in 30 ml of absolute ether was added dropwise over a period of 0.5 hour to a solution of cyclohexylmagnesium bromide prepared from 0.83 g of Mg and 5.5 g of cyclohexylbromide in 50 ml of absolute ether, with vigorous stirring and cooling to 0° during the addition. The reaction mixture was stirred for 2 hours at 0°, and then decomposed at the same temperature with 10% HCl solution (50 ml). The ether layer was separated, washed with water, dried over

anhydrous Na_2SO_4, and the ether distilled off to a small volume. A small volume of absolute alcohol was added to the resulting crystalline precipitate, and the precipitate filtered off. After two recrystallizations from ethyl acetate or alcohol-benzene mixture (9:1), 3 g (50%) of 3-cyclohexyl-$\Delta^{3,5}$-cholestadiene was obtained, with m.p. 144-146° and $[\alpha]_D^{14}$ −34.3° (105 mg substance in 10 ml $CHCl_3$ α −0.94°).

For analysis, the diene was dried in vacuo at 60° over phosphoric anhydride.

0.1236 g substance: 0.3999 g CO_2; 0.1339 g H_2O. 0.1230 g substance: 0.3976 g CO_2; 0.1320 g H_2O. Found %: C 88.10, 88.16; H 12.22, 11.92. $C_{33}H_{54}$. Calculated %: C 87.92, 12.07.

II. Synthesis of 3-Alkyl- Δ^4-cholesten-3-ols and Their Conversions.

1. Synthesis of 3-Methyl-Δ^4-cholesten-3-ol. A solution of 5.7 g of cholestenone in 35 ml of absolute ether was added dropwise at −8°, with vigorous stirring, to a solution of methylmagnesium iodide prepared from 1.4 g of Mg and 9.2 g of CH_3I in 50 ml of absolute ether. After keeping at 0° for 0.5 hour, the reaction product was decomposed at −8 to −10° by the slow addition of a solution composed of 10 g of ammonium chloride in 100 ml of water, and stirred for 0.5 hour at room temperature. The ether was separated, washed with water, dried over anhydrous sulfate and the ether distilled off in vacuo. The residue was a crystalline substance, in the form of long thin needles and had an m.p. of 102-104°. The weight was 4.7 g, which constituted about 79.6% of the theoretical, calculating for the cholestenone taken into reaction. After two recrystallizations from alcohol-ether mixture (4:1), and then from a small volume of ether, 3.5 g of the substance with m.p. 112-114° resulted with $[\alpha]_D^{16}$ +60.9° (200 mg substance in 10 mg CCl_4, α +1.29°). The substance obtained is extremely unstable with respect to heat and to traces of acids, and so it is necessary during the crystallization process to avoid prolonged heating, and to the solvents should be added a small quantity (2-3 drops) of ammonium chloride solution.

For analysis, the substance was dried in a vacuum desiccator over calcium chloride.

4.417 mg substance: 13.301 mg CO_2; 4.758 mg H_2O. 0.1040 g substance: 0.3130 g CO_2; 0.1120 g H_2O. 0.1051 g substance: 0.3153 g CO_2; 0.1146 g H_2O. Found %: C 82.17, 82.08, 82.0; H 12.05, 11.96, 12.11. M 415.2, 403.8, 402.5 (Rast). $C_{28}H_{48}O \cdot {}^1/_2 H_2O$. Calculated %: C 82.08; H 12.05; M 408.7.

2. Conversion of 3-Methyl-Δ^4-cholesten-3-ol to 3-Methyl-$\Delta^{3,5}$-cholestadiene. 5 drops of concentrated HCl was added to a solution of 2 g of 3-methyl-Δ^4-cholesten-3-ol in 150 ml of 96% ethyl alcohol, and the solution was boiled for 5 minutes. After cooling, the resulting precipitate was filtered off, washed with alcohol and dried, m.p. 77-79°. After recrystallization from alcohol-ether mixture (3:1), there resulted a substance in the form of lustrous needles, with m.p. 81.5-82° and $[\alpha]_D^{16}$ −129.8°, which did not give a melting point depression with the earlier obtained 3-methyl-$\Delta^{3,5}$-cholestadiene. Yield was 1.5 g (79.9 %).

3. Synthesis of 3-Ethyl-Δ^4-cholesten-3-ol. In a manner similar to the synthesis of 3-methyl-Δ^4-cholesten-3-ol, 4.8 g of crude 3-ethyl-Δ^4-cholesten-3-ol with m.p. 84-88° resulted from 5.7 g of cholestenone. After double recrystallization from ether by addition of a small volume of alcohol, 3.5 g of substance resulted, which crystallized in the form of long, thin needles, with a constant m.p. of 89-91° and $[\alpha]_D^{17}$ +60.6° (165 mg substance in 10 ml CCl_4, α +1.0°). As with the methyl derivative, 3-ethyl-Δ^4-cholesten-3-ol is very unstable toward heat and to the presence of traces of acids.

For analysis, the substance was dried in a vacuum desiccator over calcium chloride.

4.528 mg substance: 13.675 mg CO_2; 4.925 mg H_2O. 0.1192 g substance: 0.3584 g CO_2; 0.1306 g H_2O. Found %: C 82.42, 82.00; H 12.17, 11.98. M 421.0, 419.5 (Rast). $C_{29}H_{50}O \cdot {}^1/_2 H_2O$. Calculated %: C 82.27; H 12.06; M 423.7.

4. Conversion of 3-Ethyl-Δ^4-cholesten-3-ol into 3-Ethyl-$\Delta^{3,5}$-cholestadiene. 5 drops of conc. HCl was added to a solution of 1 g of 3-ethyl-Δ^4-cholesten-3-ol in 50 ml of 96 % ethyl alcohol, and the solution was boiled for 5 minutes. The crystalline product which resulted on cooling (lustrous crystals) was filtered off, washed and dried, m.p. 76-77°. After a single crystallization from an alcohol-ether mixture (3:1), 0.8 g of the substance resulted (88.8%), with m.p. 77-78° and $[\alpha]_D^{16}$ −119.1°, which did not give a melting point depression with the earlier-obtained 3-ethyl-$\Delta^{3,5}$-cholestadiene.

III. Synthesis of 3-Methyl-$\Delta^{3,4}$-cholestadiene and Its Conversion.

A solution of 11.4 g of cholestenone in 75 ml of ether was added, over a period of 45 minutes with vigorous stirring and cooling to −8°, to a solution of methylmagnesium iodide prepared from 2.8 g of Mg and 18.2 g of CH_3 in 100 ml of absolute ether. The reaction mass was stirred for 1 hour at 0°, and then slowly decomposed with

stirring by the addition of a solution of 20 g of ammonium chloride in 180 ml of water, without cooling, and with rapid boiling of the ether. The ether layer was separated, using anhydrous sodium sulfate, and the ether was distilled off in vacuo. The remaining light-colored viscous oil gradually crystallized upon standing. The crystalline residue was recrystallized from an alcohol-ether mixture (3:1), and the substance was obtained in the form of white lustrous plates, with m.p. 65-67°. After three recrystallizations, 8.7 g (85.9 %) of pure 3-methyl-$\Delta^{3,4}$-cholestadiene resulted, with a constant m.p. of 68-69° and $[\alpha]_D^{15}$ −12.5° (0.1437 g substance: 10 ml $CHCl_3$, α −0.17°).

For analysis, the product was dried in a vacuum desiccator over phosphoric anhydride.

3.946 mg substance: 12.766 mg CO_2; 4.271 mg H_2O. 4.953 mg substance: 15.996 mg CO_2; 5.341 mg H_2O. Found %: C 88.27, 88.13; H 12.11, 12.07. $C_{28}H_{48}$. Calculated %: C 87.88; H 12.12.

0.5 ml of conc. HCl was added to a solution of 1.4 g of 3-methyl-$\Delta^{3,4}$-cholestadiene in 200 ml of 96% ethyl alcohol and the solution was boiled for 5 minutes. The resulting lustrous white needles obtained on cooling were filtered off, washed with alcohol and dried. Weight was 1.3 g, m.p. 79-80°. After recrystallization from alcohol-ether mixture (3:1), 1.2 g of the substance with m.p. 81-82° and $[\alpha]_D^{15}$ −129.3° resulted, which did not give depression in melting point with the earlier-obtained 3-methyl-$\Delta^{3,5}$-cholestadiene. The yield was quantitative.

SUMMARY

1. The Grignard reaction between certain AlkMgX compounds and Δ^4-cholestenone has been studied.

2. By means of direct acid decomposition of the interaction products from alkylmagnesium halides and the cholestenone, a series of 3-alkyl-$\Delta^{3,5}$-cholestadienes has been obtained.

3. Under specified conditions of decomposition of the Grignard complex, 3-methyl-Δ^4-cholesten-3-ol, 3-ethyl-Δ^4-cholesten-3-ol and 3-methyl-$\Delta^{3,4}$-cholestadiene have been obtained. It has been demonstrated that these compounds when treated with an alcoholic solution of hydrogen chloride, are able quantitatively to convert into the corresponding 3-alkyl-$\Delta^{3,5}$-cholestadienes.

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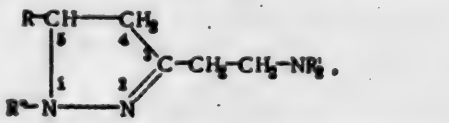
ABSORPTION SPECTRA AND STRUCTURES OF LOCAL-ANESTHETIC DERIVATIVES OF PYRAZOLINE

N. A. Valyashko and I. T. Depeshko

SYNTHESES

Compounds of the pyrazoline group, having the general formula (I):



(I)

in which R = phenyl, substituted phenyl, furyl-2, and NR'_2 = piperidino or dialkylamino groups, possess in a majority of cases, according to Sinha [1] a powerful local-anesthetizing action with a lower toxicity than cocaine, and cause but little irritation. Of this series, the most effective was found to be the 2'-n-butoxy compound.

On the basis of this data, the authors elected to synthesize, in the form of the hydrochloride salt, 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline as a representative of these new local-anesthetizing agents.

For spectrophotometric comparison, 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride was also prepared, using benzalacetone.

Benzalacetone was prepared according to Schmidt [2] from benzaldehyde and acetone. The resulting benzalacetone was distilled at 137-140°, 16 mm, and after standing for some time, solidified to crystals with m.p. 41°. According to Claisen and Ponder [3], the b.p. is 151-153° at 25 mm, with a m.p. of 41-42°.

1-N-Piperidino-5-phenyl-Δ^4-penten-3-one hydrochloride was synthesized according to the method of Mannich and Schutz [4] by condensing benzalacetone with paraformaldehyde and piperidine hydrochloride [5]. The substance obtained was readily soluble in water, chloroform, but did not dissolve in acetone, or ethyl acetate. M.p. 180.5°. Yield was 94.6%.

The phenylhydrazone of 1-N-piperidino-5-phenyl-Δ^4-pentene-3-one hydrochloride was obtained according to Mannich and Schutz [4] and Nisbet [6]. After recrystallization from 95% alcohol, the resulting yellow needles melted at 169°. The above-indicated phenylhydrazone was isomerized to the 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride. The white needles were recrystallized from absolute alcohol, m.p. 197°.

1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride was prepared according to Levvy and Nisbet [7], proceeding from 2-hydroxybenzalacetone, prepared according to Harris [8] from salicylic aldehyde and acetone. Recrystallization was carried out with benzene and animal charcoal. Crystals resulted with a m.p. of 139°; according to Tiemann and Kees [9], m.p. is 139°. 2-n-Butoxybenzalacetone was prepared from 2-hydroxybenzalacetone by conversion to the phenolate and reacting with n-butyl bromide, or n-butyl-p-toluenesulfonate, the latter giving the better result. 2-n-Butoxybenzalacetone had a b.p. of 171.5° at 3 mm.

1-N-Piperidino-5-(2'-n-butoxyphenyl)-Δ^4-penten-3-one hydrochloride was synthesized according to Levvy and Nisbet [7]. The resulting white needles had a m.p. of 164.5° after recrystallization from alcohol. Yield was 28%.

15 g of the above-indicated aminoketone hydrochloride was dissolved in 120 ml of 95% alcohol, 7 g of phenylhydrazine added, and then 7.5 g of glacial acetic acid. Upon heating to 40° for a certain length of time, yellow phenylhydrazone needles separated. After recrystallization from alcohol, m.p. was 155.5°; according to Levvy and Nisbet, m.p. is 154-155°. The phenylhydrazone was isomerized with the help of glacial acetic

acid, according to Levvy and Nisbet [7], to the 1-phenyl-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride, m.p. 19°. Yield 77%.

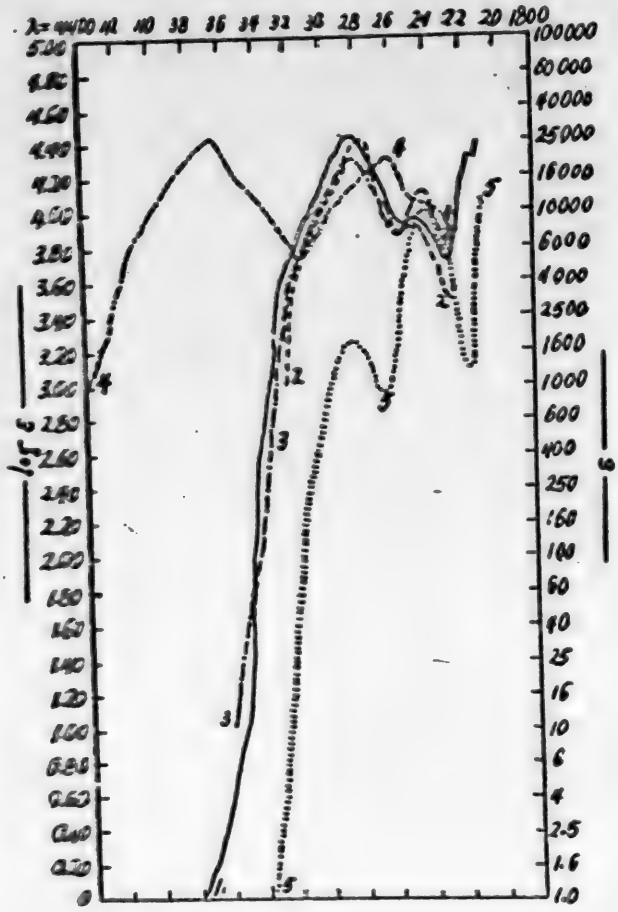
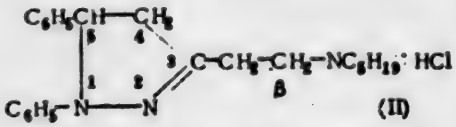


Fig. 1. 1) 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} - 10^{-5} molar; 2) the same from 10^{-4}-10^{-5} molar after standing 24 hours; 3) the same in dichloroethane, from 10^{-2}-$5 \cdot 10^{-5}$ molar; 4) 1-piperidino-5-phenyl-Δ^4-penten-3-phenylhydrazone hydrochloride in alcohol, from 10^{-4}-10^{-5} molar 5) phenylhydrazine in alcohol from 10^{-1} to 10^{-4} molar.

Absorption Spectra

1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride (II) was investigated in alcoholic concentrations ranging from 10^{-1} to 10^{-5} molar (Fig. 1, Curve 1).



(II)

After standing for 24 hours, the same solution (Fig. 1, Curve 2) gave an absorption spectrum in which the first band was shifted 60 A toward the shorter wave lengths and the absorption minimum following the second band was decreased 1.6 times. 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride was studied in dichloroethane, in a concentration range from 10^{-2} to $5 \cdot 10^{-5}$ molar (Fig.1, Curve 3). The band from λ = 2420 A and ϵ = 12000 was more pronounced than in alcoholic solution and increased in intensity 1.3 times.

From a comparison of the absorption spectra (Table 1) of 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline in alcohol and in dichloroethane with the absorption spectrum of phenylhydrazine in alcohol (Fig. 1, Curves 1,2,3 and 5), it can be seen that the second band of the pyrazoline derivative corresponds to the second band of phenylhydrazine in position, but its maximum in dichloroethane solution is more intense. As far as the first pyrazoline derivative band is concerned, it is more intense than phenylhydrazine, by 16 times, and considerably wider. It is possible that this band is complex.

The absorption spectrum given here (Fig. 1, Curve 4) for 1-piperidino-5-phenyl-Δ^4-penten-3-phenylhydrazone hydrochloride (III), from which was obtained the investigated pyrazoline derivative, gave indication of a wide, intense band in a 10^{-4} - 10^{-5} molar alcoholic solution, which may be related to the hydrazone structure of the unsaturated compound, and two bands corresponding to the pyrazoline derivative bands, while the first band is displaced 220 A to the short wave lengths, and almost merges with the second band, defined here by the bend in the curve.

$$C_6H_5-CH=CH-\underset{\underset{C_6H_5-NH-N}{\|}}{C}-CH_2-CH_2-NC_5H_{10}\cdot HCl \qquad \text{(III)}$$

TABLE 1

Name	Hydrazone band		First band		Second band	
	λ	ε	λ	ε	λ	ε
1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol			2825	25000	2473	9000
The same in dichloroethane			2825	20000	2420	12000
Phenylhydrazine in alcohol			2828	1600	2410	9000
1-Piperidino-5-phenyl-Δ^4-pentem-3-phenylhydrazone in alcohol	3675	25000	2605	20000	2370	13000

This comparison indicates that both bands of the pyrazoline derivative are already present in the phenylhydrazone, and consequently are not the result of pyrazoline ring closure.

1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcoholic solution, from $2.5\cdot10^{-4}$ to $2.5\cdot10^{-5}$ molar plus 0.01M HCl (Fig. 2, Curve 3) gave a curve parallel to the alcoholic curve (Fig. 2, Curve 1) which possessed band maxima at λ = 2813 A and ε = 2800, and at λ = 2515 A and ε = 14000. The same solution, $4\cdot10^{-5}$ molar + 0.01 M HCl (Fig. 2, curve 2), after standing for 24 hours, also gave two bands, more definitely separated, but the first band somewhat decreased and shifted toward the longer wave lengths; the second band more intense and shifted toward the shorter wave lengths. In a 5M solution of HCl, at concentrations from 10^{-1} to $5\cdot10^{-5}$ molar (Fig. 2, Curve 4), the above-mentioned pyrazoline gave an absorptions similar to the curve in the presence of 0.01M HCl, but shifted somewhat to the shorter wave lengths.

1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} to 10^{-5} molar + 10M $NaOC_2H_5$ (Fig. 3, Curve 2) gave an absorption curve shifted somewhat below that of the alcoholic curve, to the longer wave lengths; the first band maximum was decreased 1.6 times. In a $5\cdot10^{-5}$ molar solution + 10 M $NaOC_2H_5$, after 24 hours standing (Fig. 3, Curve 3), the second absorption band was decreased in intensity to ε = 5000 at λ = 2500 A and became partially overlapping with the first band. Curve 4 (Fig. 3) in 2M-sodium alcoholate was somewhat different in shape from Curve 2 (Fig. 3) in alcoholic solution + 10M $NaOC_2H_5$, both bands being displaced to the longer waves, and having a maximum at λ = 2825 A, ε = 12500 and λ = 2500 A, ε = 7625, while the absorption minimum below the second band was increased at the same time.

It can be seen from Table 2 that the general character of the spectrum in alcohol was preserved, but the intensity of both bands was considerably changed under the effect of alcoholic HCl, increasing at first, and then with a decreased intensity of the two bands with HCl excess. This indicated, possibly, entrance of the N-atom (2) of the pyrazoline ring into reaction with HCl. The absorption spectrum in sodium alcoholate solutions belongs to the free base, 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline.

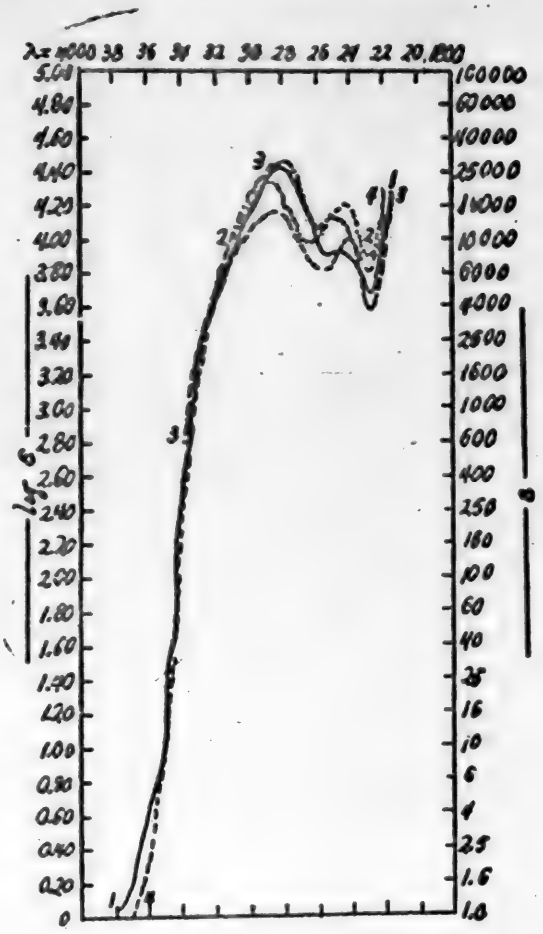


Fig. 2. 1) 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} to 10^{-5} molar; 2) the same, $4\cdot10^{-5}$ molar + 0.01 molar HCl, after 24 hours standing; 3) the same, from $2.5\cdot10^{-4}$ - $2.5\cdot10^{-5}$ molar + 0.01M HCl; 4) the same, in 5M alcoholic HCl, from 10^{-1} to $5\cdot10^{-5}$ molar.

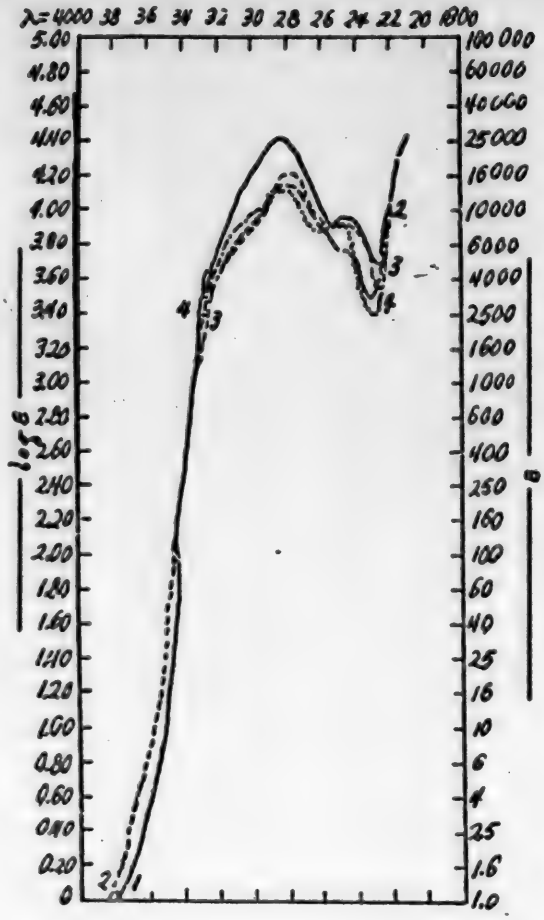


Fig. 3. 1) 1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol, from 10^{-1} to 10^{-5} molar; 2) the same, from 10^{-1} to 10^{-5} molar + 10M $NaOC_2H_5$; 3) the same, $5 \cdot 10^{-5}$ molar + 10M $NaOC_2H_5$, after 24 hours standing; 4) the same, in 2M $NaOC_2H_5$, from $4 \cdot 10^{-5}$ molar.

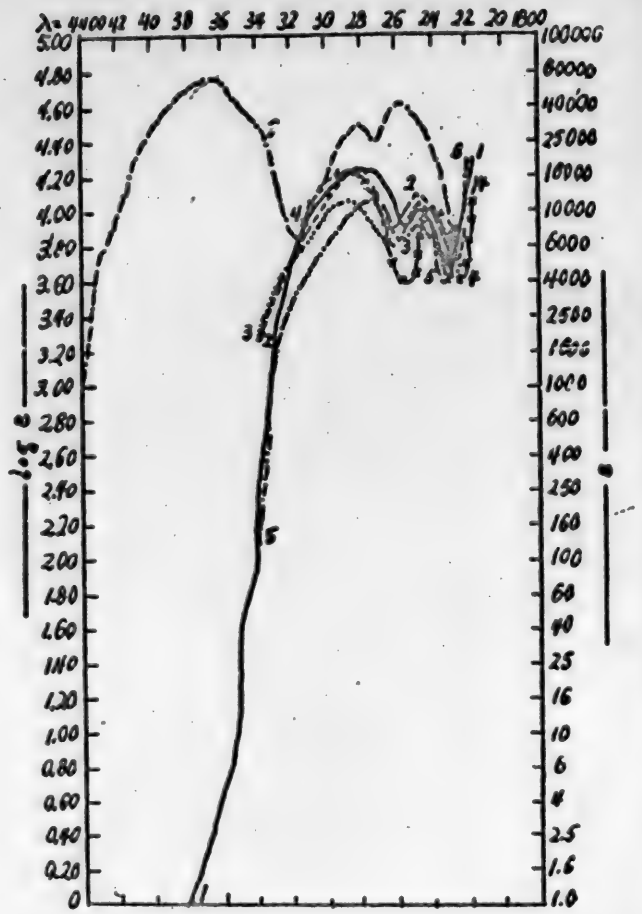
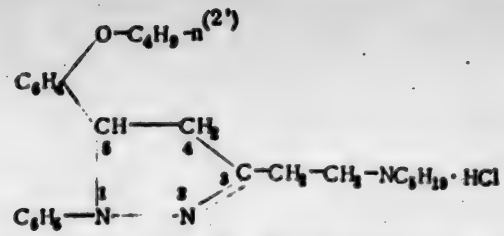


Fig. 4. 1) 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol from 10^{-4} to 10^{-5} molar; 2) the same, $5 \cdot 10^{-5}$ molar, after 24 hours standing; 3) the same, in water, $5 \cdot 10^{-5}$ molar; 4) the same, in hexane, from $4 \cdot 10^{-5}$ to 10^{-5} molar; 5) the same, in dichloroethane, from 10^{-5} to $5 \cdot 10^{-5}$; 6) 1-piperidino-5-(2'-n-butoxyphenyl)-Δ^4-penten-3-phenylhydrazone hydrochloride in alcohol, from 10^{-4} to 10^{-5} molar.

TABLE 2

Name	First band		Second band	
	λ	ε	λ	ε
1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol	2825	25000	2473	9000
The same, + 0.01M HCl	2813	28000	2515	14000
The same, + 0.01 M HCl, after 24 hours standing	2885	20000	2425	16000
The same in 5M HCl	2850	14000	2415	10000
The same, + 10M $NaOC_2H_5$	2800	16000	2518	8000
The same, + 10M $NaOC_2H_5$, after 24 hours standing	2825	12000	2560	5500
The same, in 2M $NaOC_2H_5$	2800	12500	2560	7525

1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride (IV). This was studied in alcohol, in the concentration range from 10^{-1} to 10^{-5} molar. (Fig. 4, Curve 1), and the same solution in alcohol, at $5 \cdot 10^{-5}$ molar (Fig. 4, Curve 2), did not change after standing 24 hours; Curve 3 (Fig. 4) for the same pyrazoline salt in water, at $5 \cdot 10^{-5}$ molar concentration, showed a decrease in the intensity of absorption maximum by about 1.6 times, as compared with the alcoholic curve. 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-



(IV)

pyrazoline hydrochloride also formed two absorption bands when studied in hexane solution at $4 \cdot 10^{-5}$ molar concentration (Fig. 4, Curve 4), and in dichloroethane solution from 10^{-3} to $5 \cdot 10^{-5}$ molar (Fig. 4, Curve 5), but the first band in dichloroethane, as compared with the alcoholic curve, is shifted 40 A units toward the shorter wave lengths.

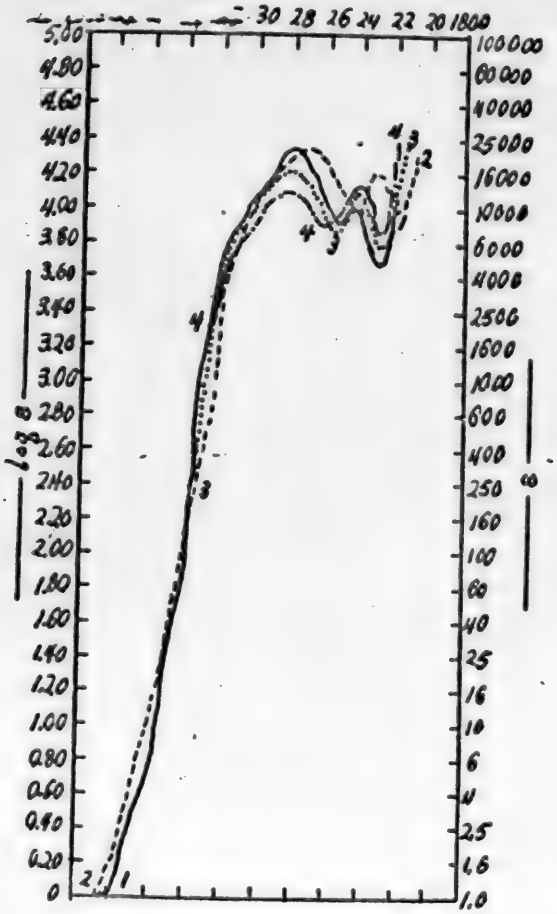


Fig. 5. 1) 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol from 10^{-4} to 10^{-5} molar; 2) the same, in 5M alcoholic HCl, from 10^{-1} to $5 \cdot 10^{-5}$ molar; 3) the same, in alcohol, from $5 \cdot 10^{-4}$ to $5 \cdot 10^{-5}$ + 0.01 M HCl; 4) the same, in 5M alcoholic HCl, from $5 \cdot 10^{-5}$M, after 24 hours standing.

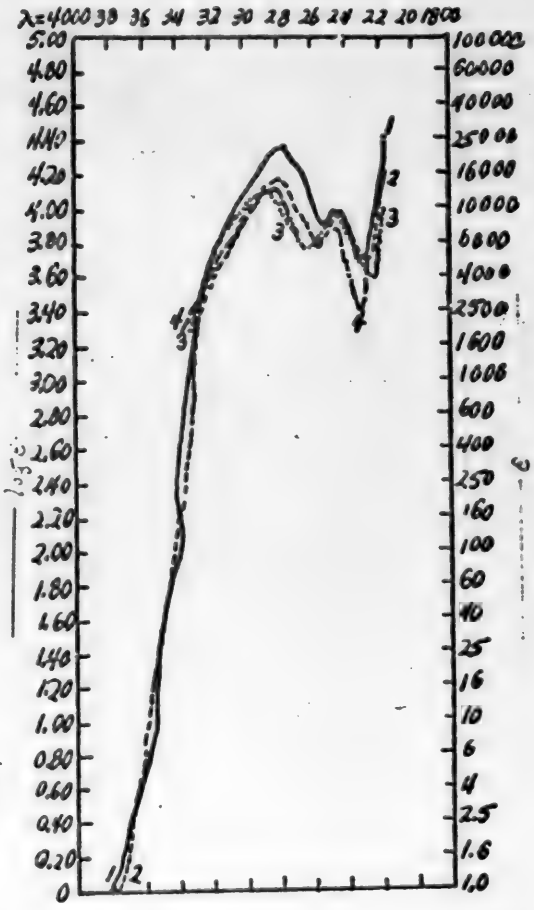
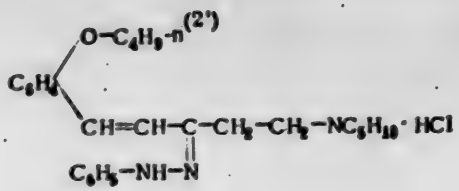


Fig. 6. 1) 1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)pyrazoline hydrochloride in alcohol from 10^{-1} to 10^{-5} molar; 2) the same, from 10^{-1} to $5 \cdot 10^{-5}$ molar + 10M $NaOC_2H_5$; 3) the same, $5 \cdot 10^{-5}$ M + 10M $NaOC_2H_5$ after 24 hours standing; 4) the same, in 2M $NaOC_2H_5$, from $5 \cdot 10^{-5}$ M.

1-Piperidino-5-(2'-n-butoxyphenyl)-Δ^4-penten-3-phenylhydrazone hydrochloride (V), in alcohol from 10^{-4} to 10^{-5} molar. (Fig. 4, Curve 6) gives three absorption bands – a hydrazone band maximum at λ = 3670 Å and ϵ = 50000 and the following two bands at λ = 2820 Å and ϵ = 30000 and at λ = 2580 Å and ϵ = 40000. Both of these bands



(V)

correspond to the pyrazoline derivative, but the first band differs sharply in intensity two-fold, and the second band four-fold. Thus, there occurs a very strong absorption in the range of these bands under the influence of the 2'-n-butoxy group in the phenylhydrazone of the ketone. Upon closure of the pyrazoline ring, the absorption drops and becomes even lower for the first band than for the pyrazoline derivative without the butoxy group, as comparison in Table 3 indicates.

A comparison of the butoxy derivative bands in various solvents indicated a considerable sensitivity toward solvents, but it was not possible to establish any definite relationship to the solvent polarities. The absorption spectrum for 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in 5M-alcoholic hydrogen chloride solution, from 10^{-1} to $5 \cdot 10^{-5}$ molar concentrations (Fig. 5, Curve 2), is expressed by a curve parallel to the alcoholic, shifting from one side to the other, but the band maxima are shifted about 100 A units toward the shorter wave lengths. Curve 4 (Fig. 5) obtained for a 5M olution of hydrogen chloride after 24 hours standing, becomes similar to the curve obtained in the presence of 0.01 M HCl, except that the minimum between the bands is decreased.

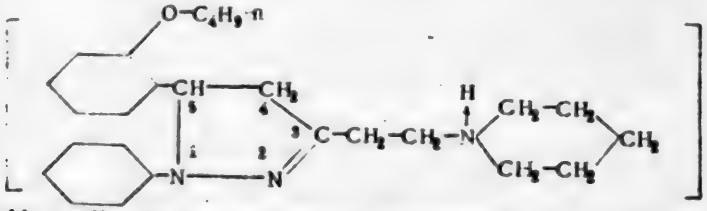
Upon investigating 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride from 10^{-1} to $5 \cdot 10^{-5}$ molar, in alcohol + 10M $NaOC_2H_5$ (Fig. 6, Curve 2), and in $5 \cdot 10^{-5}$ molar solution + 10M $NaOC_2H_5$ (Fig. 6, Curve 3) after 24 hours standing, it was found that the curve did not change, but shifted somewhat toward the shorter wave lengths. Curve 4 (Fig. 6) for a solution in 2M sodium alcoholate, $5 \cdot 10^{-5}$ molar, is very similar to Curve 3, but the maximum for the second band is decreased. No particular changes were found upon investigating this solution after 24 hours standing. Upon comparing the curves in Fig. 6, with the alcoholic curve, it can be seen that the sodium alcoholate effect leads to a weakening of the absorption bands and shifts them somewhat toward the shorter wave lengths.

TABLE 3

Name	Hydrazone band		First band		Second band	
	λ	ε	λ	ε	λ	ε
1,5-Diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol			2825	25000	2473	9000
1-Phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride in alcohol			2805	16000	2440	10000
The same, in water			2835	10000	2475	8000
The same, in hexane			2865	16000	2405	10000
The same, in dichloroethane			2765	10000	2468	10000
1-Piperidine-5-(2'-n-butoxyphenyl)-Δ⁴-penten-3-phenylhydrazone hydrochloride in alcohol	3670	50000	2820	30000	2580	40000

Evaluation of the Spectrophotometric Data

Spectrophotometric investigations of the local anesthetic, 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride (VI):



(VI)

make it possible to offer the following concept. Salt formation should proceed at the nitrogen of the more basic

piperidine ring. Due to saturation of a portion of the molecule, its absorption spectrum is not reflected in that of the diphenylpyrazoline derivative. Since both bands of the diphenylpyrazoline derivative are present in the absorption spectrum of the phenylhydrazone from which the pyrazoline derivative is obtained, these bands therefore do not belong to the pyrazoline ring. From the fact that the second band in the 1,5-diphenylpyrazoline derivative corresponds quite accurately to the second band of phenylhydrazine, a deduction can be made concerning the contribution of the phenylhydrazine portion to the diphenylpyrazoline derivative spectrum, where nitrogen atoms 1 and 2 interact with the benzene ring, as with phenylhydrazine.

The first band of 1,5-diphenylpyrazoline derivatives differs by a considerably greater intensity from that of the first band of phenylhydrazine. From this fact its participation in formation of the second phenyl group also follows, with substitution in the 5th position of the pyrazoline ring. Its interaction with the pyrazoline ring and the N atom can occur only through the group $-\underset{|}{C}H-$. This case requires an additional spectrophotometric investigation. According to Levvy and Nisbet's investigation [10], of unsaturated piperidinoketones, from which the pyrazolines were prepared, it was found that they possess a local anesthetizing action, but are highly irritating [10]. The phenylhydrazine derivatives also possess local anesthetizing action; for example, antipyrine and tolupyrine [11], p-carbethoxyphenylhydrazine $C_2H_5OCOC_6H_4NHNH_2$ are good anesthetics [12].

In view of this fact, two atomic groupings in the molecule of the pyrazoline derivative should possess local-anesthetizing properties: the first corresponding to the unsaturated piperidinoketone hydrochloride salt with 2'-n-butoxyphenyl-(5) in the piperidine ring, and the second, corresponding to the phenylhydrazine structure.

The high local-anesthetizing action of 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride is dependent upon a combination of these two local-anesthetizing groups.

SUMMARY

1. The synthesis of a new, highly-active local anesthetic, 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride, and also of 1,5-diphenyl-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride, has been worked out.

2. Their absorption spectra have been investigated in alcohol, hexane, dichloroethane, water, in alcoholic solutions of hydrogen chloride, and of sodium alcoholate, and, in addition, the absorption spectrum for phenylhydrazine in alcohol.

3. By a spectrophotometric investigation, three strong absorption bands for the phenylhydrazones, and two strong bands for pyrazoline have been determined; thus absorption spectra can serve for their differentiation, which frequently is difficult to do chemically.

4. It has been established that the absorption bands for the investigated pyrazoline derivatives are not solely dependent upon interaction of the phenyl radicals with the nitrogen atoms of the pyrazoline ring.

5. A theory has been suggested that the high local-anesthetizing action of 1-phenyl-5-(2'-n-butoxyphenyl)-3-(β-N-piperidinoethyl)-pyrazoline hydrochloride is conditioned by a combination of two groupings of atoms between 2'-n-butoxyphenyl-(5) and the piperidine ring, and a part of which corresponds to the phenylhydrazine group on the pyrazoline ring.

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CHEMICAL STRUCTURE AND PARASITICIDAL ACTIVITY

XII. DICHLOROISOMERIC MESO-ALKYLAMINOALKYLAMINOACRIDINES AND THEIR ANTIMALARIAL PROPERTIES

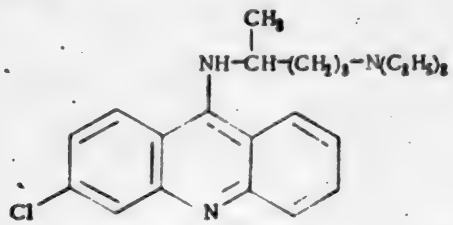
A. F. Bekhli

In the preceding work from the author's laboratory [1] there was described the synthesis for a series of physiologically-active, alkoxy-free compounds of the acridine series, which showed, upon comparison with their alkoxyl analogs, activity.

This deduction was made on the basis of a comparison of the properties of compounds of this type; as the essence of the present work, however, is the significant fact that 6-chloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine (methoxyl-free atebrin) (I) is almost equal to atebrin in its antimalarial activity.

On the other hand, among the group of chloroisomeric 9-(4'-diethylamino-1'-methylbutyl)-aminoacridines [2] synthesized by the author, 1-chloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine (II) exceeded by approximately 40% the antimalarial action of atebrin.

In 1946 an article by Spaulding and co-workers [3] appeared, concerning the synthesis of 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine (III), which possessed an antimalarial action, by test with P. gallinaceum, which exceeded that of atebrin.



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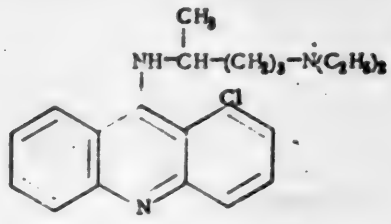

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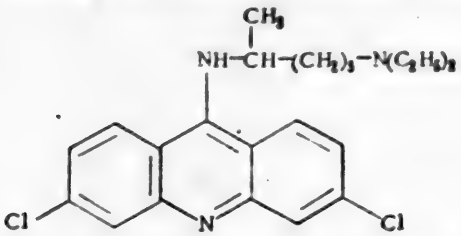
From a comparison of this work with the data given above, it seemed expedient to the author to synthesize that group of dichloroisomers of 9-dialkylaminoalkylaminoacridines wherein one chlorine is in the 6-position, i.e., in one benzene portion of the acridine nucleus, and the second is introduced in various positions of the second benzene portion of the acridine nucleus. From a knowledge of the activity of methoxyl-free atebrin (I) which contains chlorine in the 6-position, it is possible to determine how the introduction of a second halogen will affect the antimalarial activity of the corresponding acridine derivative. Therefore, the following compounds were selected for synthesis:



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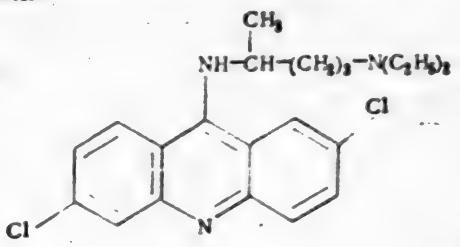

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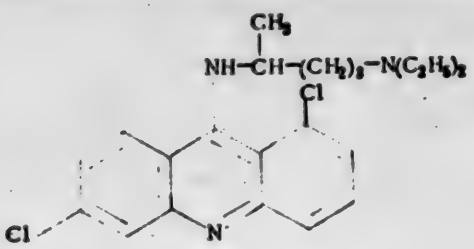

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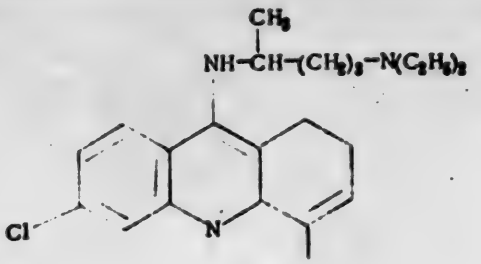

(VI)

It should be mentioned that Spaulding and co-authors, during synthesis of 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, obtained an intermediate 3,6,9-trichloroacridine by condensing 4-chloro-2-nitrobenzaldehyde with chlorobenzene, with subsequent treatment of the resulting 3,6-dichloroacridone by phosphorous oxychloride. The American authors preferred this procedure to the Uhllmann reaction from 2,4-dichlorobenzoic acid and m-chloroaniline, because of the low yield of 3,5'-dichlorodiphenylamino-2'-carboxylic acid (5.8%) which was simultaneously obtained.

The authors pointed out another limitation of the Uhllmann condensation, namely, that they foresaw the task of separating the isomeric trichloroacridines which would result upon treatment of 3,5'-dichlorodiphenylamine-2'-carboxylic acid with phosphorous oxychloride —ring closure occurring in the o- and p-positions with regards to the substituent present in the ring.

Nevertheless, the author decided to synthesize the selected compounds (III IV) by the method which was abandoned by the American authors mentioned. By carrying out the Uhllmann reaction in an aqueous medium under conditions developed by the author, it was possible to increase to 53% (Spaulding gave 5.8%) the yield of 3,5'-dichlorodiphenylamino-2'-carboxylic acid.

The resulting acid, upon heating with phosphorous oxychloride, was converted into a mixture of the isomeric 1,6,9- and 3,6,9-trichloroacridines. Separation of the isomers was effected by the established fact that the resulting isomeric trichloroacridines vary in their solubility with regard to alcoholic ammonia. It was found that 1,6,9-trichloroacridine goes into solution, while 3,6,9-trichloroacridine remains insoluble.

It was noted that chlorine in position 9 of both 1,6,9- and 3,6,9-trichloro-acridines possesses a high mobility, and that the products, upon standing even for brief time in air, will convert into acridone, the greatest mobility being for the first isomer.

It was found that if the mixture of isomeric trichloroacridines was not separated, and then, after standing for a short time in air, condensed with a side chain, that a considerable quantity of acridone was then isolated; it was possible to isolate, then, as the condensation product, pure 3,6-dichloro-9(4'-diethylamino-1'-methylbutyl)-aminoacridine. If the dichloroacridone separated during the reaction is converted by phosphorous oxychloride into the trichloroacridine, there then results a product which, according to its melting point, corresponds to 1,6,9-trichloroacridine. This example illustrates clearly that the meso-halogen in 1,6,9-trichloroacridine has a greater mobility than in 3,6,9-trichloroacridine.

The separated isomeric trichloroacridines were condensed with 1-diethylamino-4-aminopentane in phenol, and there were separated dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines (III and IV), in the form of the dihydrochlorides, with melting points, respectively, of 230-231° and 183-184°. From dihydrochloride (III) the base, 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was separated in the crystalline form, m.p. 81°.

If the freshly-prepared isomeric mixture of trichloroacridines is not separated, but, instead, immediately condensed with 1-diethylamino-4-aminopentane, then an isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl) aminoacridines results, the dihydrochloride of which melts at 210-212°.

2,6- and 4,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines (V and VI) were obtained in the usual manner by condensing the corresponding 2,6,9- and 4,6,9-trichloroacridines with 1-diethylamino-4-aminopentane in phenol.

The indicated trichloroacridines were prepared by ring closure of 4,5'- and of 2,5'-dichlorodiphenylamino-2' carboxylic acids with phosphorous oxychloride. The isomeric dichlorodiphenylaminocarboxylic acids were obtained by condensing 2,4-dichlorobenzoic acid with o- and p-chloroanilines. The dihydrochloride of 2,6-dichloro-9-(4'-

diethylamino-1'-methylbutylene)-aminoacridine, and the corresponding intermediate products, have been described by O. Yu. Magidson, A.M. Grigorovsky and E. Galperin [4]. The author has isolated for the first time the base, 2,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine.

The described compounds, in the form of their hydrochloride salts, were tested for their antimalarial action on an avian malaria. The effectiveness was determined with regards to the erythrocytic stages of the parasite during Plasmodium relictum blood infection. It was found at the time that the isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine possessed the greatest activity, the 3,6-dichloroisomer a greater activity than that of atebrin, the 2,6-dichloroisomer active, but less so than atebrin, and finally the 4,6-dichloroisomer, which was found to be completely inactive. With in vivo toxicity studies on mice, the 3,6- and 1,6-dichloroisomers, as well as the isomeric mixture, were found to be less toxic than atebrin; the 2,6-dichloroisomer was found to be more toxic than atebrin.

These tests were carried out in the protozoological division of the institute by Prof. Sh. D. Moshkovsky and the senior, scientific worker, S.A Syrkina, to whom the author expresses his appreciation.

EXPERIMENTAL

3,5-Dichlorodiphenylamino-2'-carboxylic Acid. 78 g of 2,4-dichlorobenzoic acid, 100 g of m-chloroaniline, 30 g of potash, 70 ml of water and 1 g of copper acetate were heated at the boiling point for 21 hours (temperature in the flask was 110-120°).

After removal of unreacted m-chloroaniline (62 g) by steam distillation, the residue was heated with animal charcoal, filtered and acidified with hydrochloric acid to a neutral reaction. 61.2 g, or 53% of theory yield, of 3,5'-dichlorodiphenylamino-2'-carboxylic acid was isolated; after recrystallization from aqueous alcohol, the acid melted at 196° (Spaulding indicated 196-198°). Upon acidification of the filtrate to an acid reaction, 26.5 g of 2,4-dichlorobenzoic acid, which did not enter into reaction, was isolated.

The Mixture of 1,6,9- and 3,6,9-Trichloroacridines and Its Separation. 30 g of 3,5-dichlorodiphenylamino-2'-carboxylic acid, 50 ml of chloroform and 20 ml of phosphorous oxychloride were heated for 4 hours on a water bath. After distilling off the chloroform, the residue was poured onto ice, treated with ammonia, filtered with suction and washed with water. 30 g of crude product was isolated (or 99% of theoretical yield), which represented a mixture of 1,6,9- and 3,6,9-trichloroacridines.

The resulting mixture of isomers was heated in water-alcoholic ammonia (300 ml of alcohol + 30 ml of 25% ammonia) to boiling and the hot solution filtered off; the 3,6,9-trichloroacridine remained on the filter and the 1,6,9-trichloroacridine went into solution.

16.4 g of 3,6,9-trichloroacridine resulted, which, after crystallization from heptane, and upon immersion of the capillary into preheated sulfuric acid, melted at 220° (Spaulding gives 225°).

After addition of water to the alcoholic-ammoniacal filtrate, 1,6,9-trichloroacridine precipitated (5.6 g), which, after crystallization from heptane, melted at 144-146°.

8.200 mg substance: 0.382 ml N_2 (21°, 756 mm). 9.071 mg substance: 0.412 ml N_2 (21°, 756 mm). Found %: N 5.32, 5.24. $C_{13}H_6NCl_3$. Calculated %: N 4.95.

1,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. To a melt, consisting of 15 g of phenol and 4.0 g of 1-diethylamino-4-aminopentane, was added with vigorous stirring, finely-ground 1,6,9-trichloroacridine (6.3 g), while heating on a boiling water bath. The mixture was heated for 1 hour, and was then poured into a 10% solution of caustic soda. The separated oil was washed twice with water and dissolved in benzene, and the 1,6-dichloroacridone (0.7 g) formed during the reaction was filtered off. The benzene solution was dried with potash. After removal of the potash, alcoholic hydrochloric acid was added to the benzene solution to a Congo reaction. The hydrochloride separated as an oil, which, after solution in absolute alcohol with the addition of ether, and standing, crystallized. The product was filtered by suction, washed with acetone. The yield was 3 g, m.p. 179-180°.

1,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine hydrochloride crystallized out from alcoholic-ether mixture in the form of fine, yellow prisms, with m.p. 183-184°.

The product was soluble in water and alcohol, [illegible] dissolve in ether or acetone.

0.1999 g substance: 0.0081 g H_2O. 0.2566 g substance: 0.0095 g H_2O. Found %: H_2O 4.05, 3.70. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot H_2O$. Calculated %: H_2O 3.63 0.2415 g substance: 0.1420 g AgCl. 6.125 mg substance: 0.499 ml N_2 (27°, 746 mm). 5.588 mg substance: 0.460 ml N_2 (27°, 746 mm). Found %: Cl(ionic) 14.54; N 9.09, 9.19. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.86; N 8.80.

3,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. This compound resulted from 3,6,9-trichloroacridine (7.5 g) and 1-diethylamino-4-aminopentane (4.5 g) in phenol (15 g), by a procedure identical with that described above. There was separated from the reaction mass 1.6 g of 3,6-dichloroacridone: 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine dihydrochloride resulted in the form of a yellow powder, m.p. 230-231° (Spaulding gives 235°) in the amount of 3.2 g. A mixed sample with the 1,8-dichloroisomer gave a depression, melting at 169-175°.

The product was soluble in water and alcohol but did not dissolve in acetone or ether.

Found %: H_2O 3.89. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot H_2O$. Calculated %: H_2O 3.63. Found %: Cl (ionic) 14.58; N 9.11, 8.99. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.86; N 8.80.

The base, 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, was obtained by the addition of an ammonia solution to an aqueous solution of the hydrochloride; the resulting oil crystallized from aqueous acetone, m.p. 81°.

0.0772 g substance: 0.0029 g H_2O. 0.1623 g substance: 0.0072 g H_2O. 4.742 mg substance: 0.412 ml N_2 (22°, 744 mm). 4.441 mg substance: 0.392 ml N_2 (22°, 744 mm). Found %: H_2O 3.75, 4.43; N 9.84, 9.99. $C_{22}H_{27}N_3Cl_2 \cdot H_2O$. Calculated %: H_2O 4.26; N 9.95.

Condensation of a Mixture of 1,6,9- and 3,6,9-trichloroacridine with 1-Diethylamino-4-aminopentane. After standing for some time (the product partially hydrolyzing the acridone), the unseparated mixture of isomeric trichloroacridines (6 g) was condensed with 1-diethylamino-4-aminopentane (4.5 g) in phenol (15 g) by the procedure described above. 3 g of acridone was separated from the reaction mass.

1.5 g of the condensation product, in the form of the hydrochloride, with m.p. 230°, resulted, a mixed sample with 3,9-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine of which did not give a depression in melting point. From the hydrochloride solution a base was separated by 25% ammonia solution, which crystallized from aqueous acetone; m.p. 81-82°. A sample, mixed with the base, 3,9-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, did not give depression.

Hence, it may be considered that in the case given a pure product, 3,6,-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was obtained; 1,6,9-trichloroacridine, a more unstable product, was hydrolyzed to acridone. For verification of this assumption, the dichloroacridine separated from the reaction was converted, by the aid of phosphorous oxychloride, into trichloroacridine, which had an m.p. of 142°, and was found to be identical with 1,6,9-trichloroacridine.

Condensation of a Freshly-Prepared Isomeric Mixture of 1,6,9- and 3,6,9-Trichloroacridines with 1-Diethylamino-4-aminopentane (III and IV). The isomeric mixture (51.2 g) of 1,6,9- and 3,6,9-trichloroacridines (recrystallized from benzene, m.p. 190°) was added to the melt consisting of 103 g of phenol and 28 g of 1-diethylamino-4-aminopentane, with vigorous stirring and with heating on a water bath. The mixture was heated, with stirring, for an additional hour, and the mass then poured into 10% caustic soda solution. The viscous oil which separated was washed several times with water, the water poured off, and the oil dissolved in acetone. The acridone formed during the reaction did not dissolve in acetone and was filtered off.

Alcoholic hydrogen chloride was added to the acetone solution, and the hydrochloride which formed separated out first as an oil, which, after some standing, and stirring with a glass rod, crystallized. The product was filtered off with suction and was washed with dry acetone. The yield of crude product varied from 62 to 82% of the theoretical. The dihydrochloride of the isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines was crystallized from aqueous acetone, dissolved in the minimal volume of water with heating, and to the solution was then added animal charcoal, the mixture filtered, and acetone added to the cooled filtrate. A fine, yellow, crystalline powder resulted, m.p. 210-212°.

2,5'-Dichlorodiphenylamino-2'-carboxylic acid. 160 g of 2,4-dichlorobenzoic acid, 200 g of o-chloroaniline, 185 g of potash, 145 ml of water and 2.26 g of copper acetate were heated on an oil bath at 140-150°

for 28 hours. After removal of the unreacted o-chloroaniline (146 g) by steam distillation, the residue was heated with animal charcoal, filtered, and acidified with hydrochloric to the neutral point. 51 g, or 21.6% of theoretical yield of 2,5'-dichlorodiphenylamino-2'-carboxylic acid was isolated.

After purification by reprecipitation and by crystallization from aqueous alcohol, the acid melted at 228-229°.

6.625 mg substance: 0.304 ml N_2 (25°, 748 mm). 6.530 mg substance: 0.333 ml N_2 (24°, 748 mm). Found %: N 5.17, 5.76. $C_{13}H_9O_2NCl_2$. Calculated %: N 4.96.

4,6,9-Trichloroacridine. 43.3 g of 2,5'-dichlorodiphenylamino-2'-carboxylic acid, 95 ml of dichloroethane and 40 ml of phosphorous oxychloride were heated for 4 hours on a water bath. After distilling off the chloroform, the residue was poured onto alkalized ice, filtered by suction and washed with water. The product crystallized from benzene. Cream-colored prisms, m.p. 177-178°, weight 24 g. Soluble in benzene, alcohol; insoluble in water.

7.623 mg substance: 0.372 ml N_2 (28°, 739 mm). 7.520 mg substance: 0.353 ml N_2 (22°, 742 mm). Found %: N 5.38, 5.30. $C_{13}H_6NCl_3$. Calculated %: N 4.95.

4,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. 11.5 g of 4,6,9-trichloroacridine was condensed with 6.3 g of 1-diethylamino-4-aminopentane in phenol (25 g) with heating on a water bath. The condensation product was poured into a solution of 10% alkali, the separated oil washed several times with water, and then dissolved in acetone. To the dried acetone solution of base, alcoholic hydrogen chloride was added to an acid Congo reaction. The oil which separated on standing solidified. The product was recrystallized from a mixture of alcohol and acetone. Fine yellow crystalline powder, m.p. 194°. Yield of pure product was 7.3 g.

The dihydrochloride was readily soluble in water and alcohol, insoluble in acetone and ether.

0.2009 g substance: 0.0080 g H_2O. 0.2022 g substance: 0.1159 g AgCl. Found %: H_2O 3.98; Cl (ionic) 14.18. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot H_2O$. Calculated %: H_2O 3.68; Cl (ionic) 14.32. 8.640 mg substance. 0.666 ml N_2 (26°, 748 mm). 6.599 mg substance: 0.540 ml N_2 (20°, 748 mm). Found %: N 8.66, 9.19. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: N 8.80.

The base, 4,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was obtained by treatment of an aqueous solution of the dihydrochloride with ammonia, the separated oil crystallizing after standing, and after recrystallization from aqueous acetone, yellow plates, m.p. 67-68° resulted. The compound was soluble in a majority of the organic solvents, and contained water of crystallization which was removed either by heating with phosphorous pentoxide at 50°, or by prolonged standing in a desiccator, whereupon the crystalline product converted to an oil.

9.141 mg substance: 0.784 ml N_2 (23°, 741 mm). 7.784 mg substance: 0.686 ml N_2 (25°, 743 mm). 0.1588 g substance: 0.0071 g H_2O. Found %: N 9.64, 9.86; H_2O 4.47. $C_{22}H_{27}N_3Cl_2 \cdot H_2O$. Calculated %: N 9.95; H_2O 4.26.

4,5'-Dichlorodiphenylamino-2'-carboxylic acid and 2,6,9-trichloroacridine were obtained by the method described by O. Yu. Magidson and coworkers [4].

2,6-Dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine. 15.3 g of 3,6,9-trichloroacridine was condensed with 5.5 g of 1-diethylamino-4-aminopentane in phenol medium (30 g) by the method described above.

4.4 g of 2,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine dihydrochloride separated. The product crystallized from aqueous acetone in the form of tetrahedral plates, which softened at 190° and melted at 226°.

0.2370 g substance: 0.0110 g H_2O. 0.2012 g substance: 0.0096 g H_2O. 7.445 mg substance: 0.539 ml N_2 (26°, 749 mm). 7.325 mg substance: 0.549 ml N_2 (26°, 747 mm). Found %: H_2O 4.64, 4.77; N 8.14, 8.40. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl \cdot 1.25\ H_2O$. Calculated %: H_2O 4.50 N 8.40. 0.2260 g substance: 0.1352 g AgCl. 0.1859 g substance: 0.1101 g AgCl. 5.682 mg substance: 0.451 ml N_2 (22°, 757 mm). Found %: Cl (ionic) 14.80, 14.65; N 9.14. $C_{22}H_{27}N_3Cl_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.86; N 8.80.

The base, 2,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridine was obtained by treatment of an aqueous solution of the hydrochloride with alkali. The product crystallized from aqueous acetone in yellow plates, m.p. 78-79°.

It dissolved in a majority of the organic solvents, but was insoluble in water.

0.1264 g substance: 0.0068 g H_2O. 6.177 mg substance: 0.549 ml N_2 (21°, 756 mm). 6.145 mg substance: 0.539 ml N_2 (21°, 756 mm). Found %: H_2O 5.38; N 10.26, 9.96. $C_{22}H_{27}N_3Cl_2 \cdot 1.25 \cdot H_2O$. Calculated %: H_2O 5.27; N 9.84.

SUMMARY

1. 2,5'-, 3,5'- and 4,5'-dichlorodiphenylamino-2-carboxylic acids have been obtained by condensing 2,4-dichlorobenzoic acid with o-, m- and p-chloroanilines. 3,5'-Dichlorodiphenylamino-2'-carboxylic acid was obtained in 53% yield of theory.

2. By the interaction of 3,5-dichlorodiphenylamino-2'-carboxylic acid with phosphorous oxychloride, there has been obtained a mixture of the isomeric 1,6,9- and 3,6,9-trichloroacridines, which have been separated on the basis of their differential solubility in aqueous-alcoholic ammonia; the remaining isomeric trichloroacridines, 2,6,9- and 4,6,9-, have been obtained by heating 4,5'- and 2,5'-dichlorodiphenylamino-2'-carboxylic acids with phosphorous oxychloride.

3. 1,6-, 2,6-, 3,6- and 4,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines, and mixture of isomers 1,6- and 3,6- dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines, have been synthesized by condensation of the corresponding trichloroacridines with 1-diethylamino-4-aminopentane.

4. The resulting dichloroisomers of 9-(4'-diethylamino-1'-methylbutyl)-aminoacridine, in the form of their hydrochloride salts, have been biologically tested with Plasmodium relictum.

According to the data of Prof. Sh. D. Moshkovsky and senior scientific -worker, S.A. Syrkina, the preparations have shown the following activities. The isomeric mixture of 1,6- and 3,6-dichloro-9-(4'-diethylamino-1'-methylbutyl)-aminoacridines and the 3,6-dichloroisomer, possess the highest activities, exceeding that of atebrin; the 1,6-dichloroisomer is approximately equal to that of atebrin, the activity of the 2,6- dichloroisomer is less than the activity of atebrin, and the 4,6-dichloroisomer possesses no antimalarial activity.

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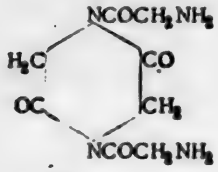
THE MICROSTRUCTURE OF PROTEIN

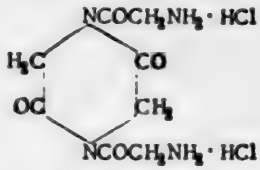
XII. SYNTHESIS OF THE FREE N-AMINOACYL COMPOUND OF DIKETOPIPERAZINE AND OF ITS DERIVATIVES

L. N. Akimova and N. I. Gavrilov

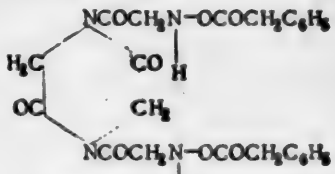
In the preceding article [1] the authors demonstrated that it was possible to synthesize the N-acylamino derivative of diketopiperazine by protecting the amino group of the amino acid through the acyl derivatives. Abderhalden [2] was the first to express his thought on the matter of a possible linkage of diketopiperazine with amino acids through nitrogen of the first. During the last 25 years of his life, he tried unsuccessfully to carry out this reaction. Apparently, his failures in this work forced him to renounce the diketopiperazine theory [3]. In the present work the authors describe the synthesis of free N,N'-diglycyldiketopiperazine (I), its HCl salt (II), its carbobenzoxyderivative (III), and the carbobenzoxy derivative of N,N'-diglycylalanine (IV):



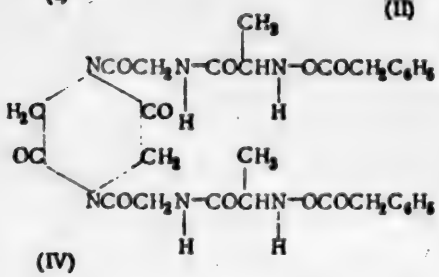
(I)



(II)



(III)

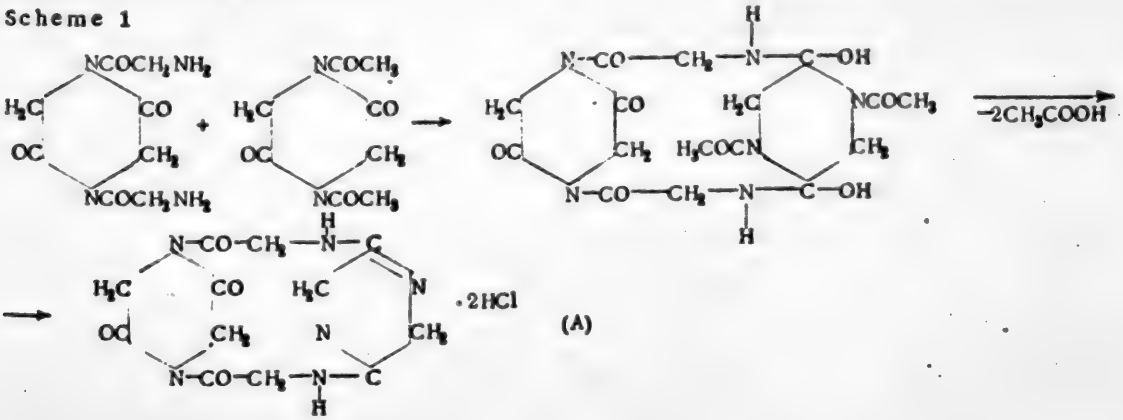


(IV)

These experiments make it possible to consider that N,N'-amino acid derivatives of diketopiperazine are easy to synthesize, and by the modern Bergmann method [4] can be elongated to form a peptide chain, but they give a biuret reaction only because of asymmetric cleavage of the ring. The authors doubt that these derivatives play an important role in the structure of the protein protoacid (S. S. Perov [5]), but it is possible that this linkage acts as a prosthetic group of the protein (S. S. Perov anticomplex). The authors have studied further both the synthesis of these linkages and the properties of model structures. It is not excluded that the complexity of the molecule approximates the properties of a peptone structure (molecular structure, Fodor acropeptide).

In our model, the synthesis of which we are carrying out at the present time, 2 diketopiperazines are linked with two tripeptides. At the moment, in N,N'-diglycyldiketopiperazine, the authors have realized a construction model of such structure, very easy to synthesize (Scheme 1, A):

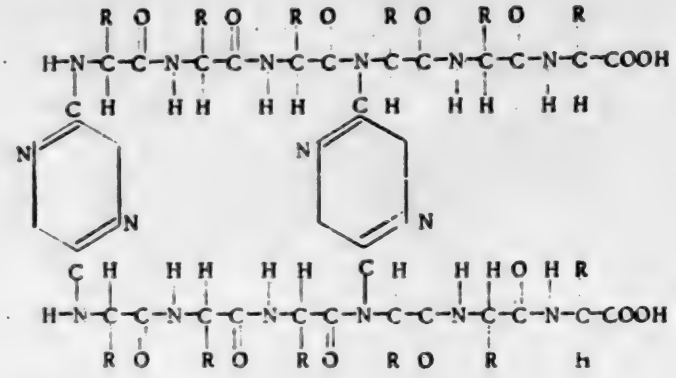
Scheme 1



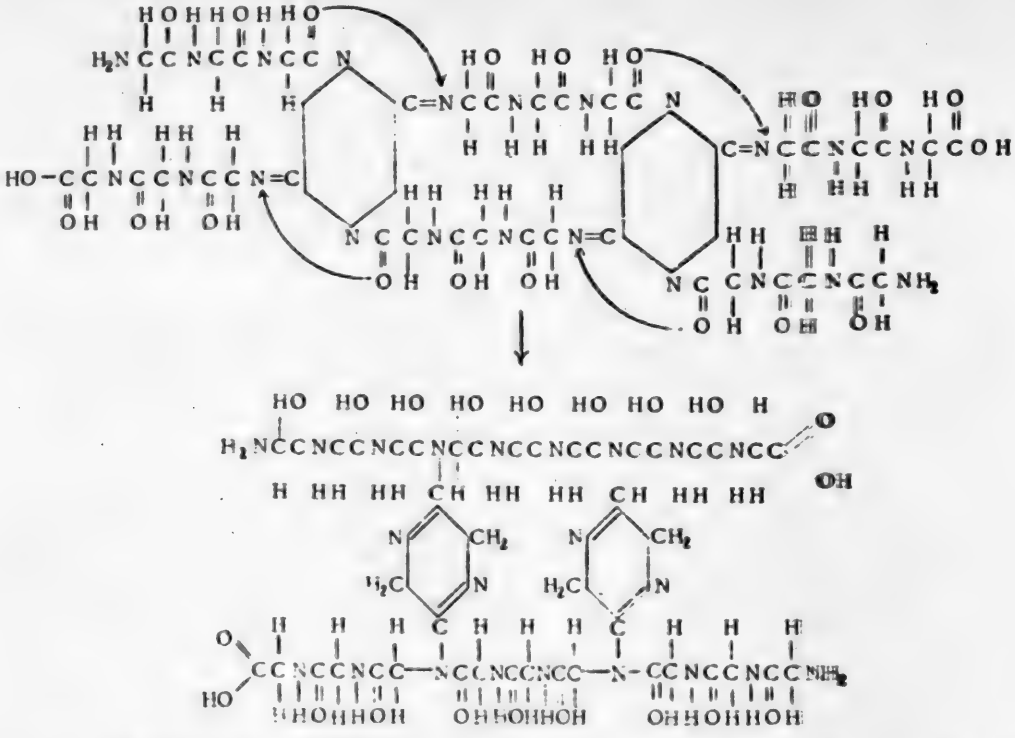
(A)

This compound shows that derivatives of N,N'-substituted diketopiperazine have free rotation and may form bridges between the diketopiperazines. This property makes certain the fact that the authors' molecular structure (2 hexapeptides linked to 2 dihydropiperazines) (vide Scheme 2), and the molecular structure on the basis of Levine's hypothesis [6], discussed elsewhere by the authors and based upon N,N'-acylaminodiketopiperazine conversions, will be shortly carried out (vide Scheme 3).

Scheme 2



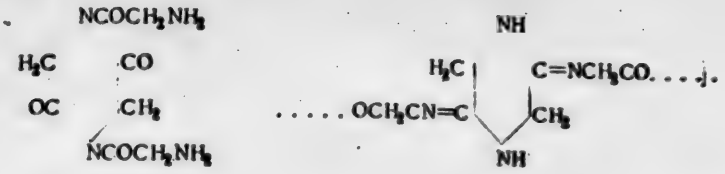
Scheme 3



In the present series, the authors' works have experimentally established two possible linkages for diketopiperazines and amino acids: 1) amidine, and 2) N-acylamine (Vide Scheme 4), which, by the same fact completely eliminates the possibility for existence of dead polypeptide structures of protein•. M. I. Plekhan's works [7] which determined the tripeptide structure of the peptide portion of protein further confirms the authors' assertions.

• Beyond the tripeptides.

Scheme 4



EXPERIMENTAL

1. Acylation of diketopiperazine by N-carboglycinealdehyde. 1.1 g of N-carboglycineanhydride, synthesized according to Leuchs [8], was ground in a mortar with 0.62 g of diketopiperazine. 20 ml of dry xylene was added and heated in Wood's metal to the cessation of CO_2 evolution (absorbant – a solution of baryta water). The precipitate was filtered and washed on the filter with cold water. A portion of the precipitate dissolved. The undissolved portion, with negative anhydride and ninhydrin reactions, gave a biuret reaction of the tripeptide type (upon standing with alkali). The aqueous filtrate from the precipitate was evaporated to dryness in vacuo with heat. By reactions (dipeptide biuret and anhydride), the resulting substance was found to be diketopiperazine. The precipitate, giving a tripeptide biuret reaction, represented a glycine polymer of unknown structure.

Upon repeating this experiment, preliminary heating of diketopiperazine with N-carboglycineanhydride was carried out on a water bath (boiling); here, no evolution of CO_2 occurred. However, an increase in temperature (heating in Woods metal at 142°) caused reaction, and strong CO_2 evolution occurred. From this experiment, as well as from the above-described, diketopiperazine and glycine polymer were isolated.

Thus the attempt directly to aminoacylate diketopiperazine, for the purpose of obtaining free N,N'-aminoacyldiketopiperazine, failed. The desire to synthesize free N,N'-diglycyldiketopiperazine led the authors to consider a different procedure. Having abandoned the attempt to synthesize this compound directly, the authors utilized its earlier-synthesized derivatives. Among the literature methods for removal of acyl groups in amino acid derivatives (peptides), the most appropriate was found to be elimination of the phthalyl substituent with the aid of hydrazine hydrate, which the authors therefore used.

2. The interaction of 1,4-diphthaiylglycyl-2,5-diketopiperazine with hydrazine hydrate. In absolute alcohol medium. a) 0.25 g (0.02 mole) of hydrazine hydrate and 30 ml of absolute ether was added to 1.22 g of N,N'-diphthalylglycyldiketopiperazine. The solution was shaken for 1 hour on a rocker. The resulting precipitate was filtered off and washed on the filter with alcohol. The precipitate and the filtrate were analyzed separately. Upon standing, a precipitate separated from the alcoholic filtrate which was filtered off and washed with ether. The substance was recrystallized from boiling 50% alcohol. The resulting precipitate did not give the anhydride and ninhydrin reactions, did not melt above 340°, and was found to be the phthalylhydrazide.

2.405 mg substance: 0.372 ml N_2 (25°, 730 mm). 2.285 mg substance: 0.365 ml N_2 (25°, 730 mm).
Found %: N 17.1, 17.2. $C_8H_5O_2N_3$. Calculated %: N 17.28.

Precipitate. This was treated with aqueous alcohol. Upon standing at room temperature, crystals separated out from the filtrate, which were filtered off and washed with alcohol and ether. Dried in vacuo over P_2O_5. The melting point by rapid heating (on a thermometer) was 245°; upon slow heating in a sealed capillary, the substance decomposed at 220°. Insoluble in water, gave the anhydride (by the usual procedure) and the ninhydrin reactions with 5-minute heating reactions. Crystalline form under the microscope – well-formed rectangles.

3.055 mg substance: 2.208 ml 0.2 N solution $KH(IO_3)_2$. 3.930 ml substance: 2.824 ml 0.2 N solution $KH(IO_3)_2$.
Found %: N 20.25, 20.12. $C_{24}H_{24}O_6N_8$.

b) 1.22 g of N,N'-diphthalylglycyldiketopiperazine was mixed with 0.5 g (0.04 mole) of hydrazine hydrate in 30 ml of absolute alcohol. The solution was shaken on a rocker for 5 hours. After completion of the reaction, the alcoholic filtrate, basic to litmus, was separated from the filtrate and washed with alcohol (to a neutral reaction in the alcoholic filtrate).

Investigation of the alcoholic filtrate. During the concentration, a substance separated which was recrystallized from 50% alcohol. Its complete analysis was carried out.

3.602 mg substance: 0.552 ml N_2 (23°, 744 mm). 7.005 mg substance: 1.067 ml N_2 (21°, 748 mm). 3.165 mg substance: 6.879 mg CO_2; 1.065 mg H_2O. 3.100 mg substance: 6.733 mg CO_2; 0.970 mg H_2O. Found %: N 17.30, 17.40; C 59.31, 59.27; H 3.76, 3.50. $C_8H_6O_2N_2$. Calculated %: N 17.28; C 59.26; H 3.70.

From analysis and properties, the substance isolated represented phthalylhydrazide.

Dry hydrogen chloride was passed through the alcoholic filtrate from the phthalylhydrazide of the basic reaction. The resulting precipitate was filtered off and washed with alcohol. M.p. 198°. By the properties (insoluble in alcohol, readily soluble in water, reducing copper during the biuret reaction, positive ninhydrin reaction) and by the melting point, the substance was found to be the hydrazine hydrochloride.

Determination of amino nitrogen according to Sorensen-Gavrilov. 0.0960 g of the substance: 9.3 ml of 0.2 N NaOH (respectively, 17.88 ml of 0.1 N H_2SO_4) Found %: N 26.67. $H_6N_2Cl_2$. Calculated %: N 26.66.

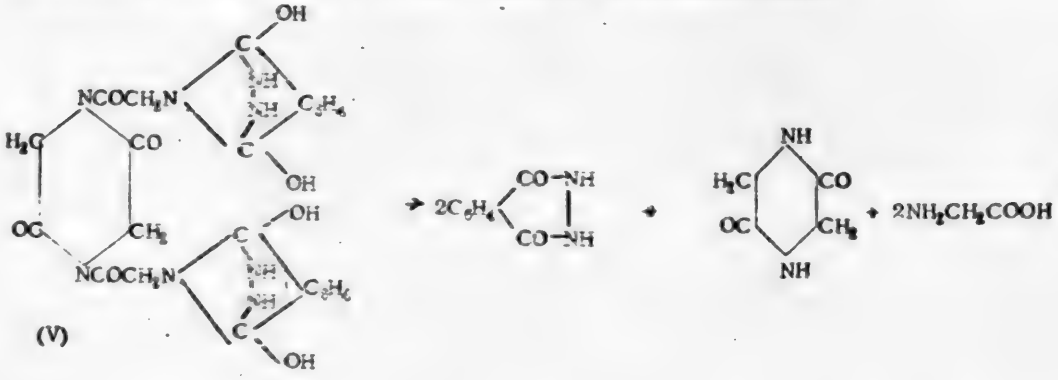
Titration according to Willstätter. 0.0894 g of the substance: 16.25 ml of 0.1 N alcoholic NaOH (respectively, 16.97 ml of 0.1 N H_2SO_4). Found %: N 26.58. $H_6N_2Cl_2$. Calculated %: N 26.66.

Treatment of the precipitate. The precipitate was treated on a filter at room temperature with 50% alcohol. Here a small portion of the precipitate was undissolved (in it were crystals of the initial substance). From the water-alcohol filtrate, upon standing for 24 hours, a substance separated which was filtered off and washed repeatedly with water (because of possible presence of diketopiperazine) and then with alcohol. Under the microscope, this substance represented very active crystals in polarized light, in the form of rectangular plates. M.p. about 220°, with decomposition. The anhydride reaction was positive, the ninhydrin: positive, on prolonged heating. A complete analysis was carried out.

1.830 mg substance: 0.007 ml N_2 (23°, 748 mm). 1.445 mg substance: 0.258 ml N_2 (23°, 748 mm). 3.010 mg substance: 5.760 mg CO_2; 1.277 mg H_2O. 3.030 mg substance: 5.795 mg CO_2; 1.277 mg H_2O. Found %: N 20.32, 20.36; C 52.23, 52.19; H 4.27, 4.25. $C_{16}H_{14}O_8N_4$. Calculated %: N 20.29; C 52.17; H 4.35.

The substance isolated did not give depression with one obtained from experiment "a".

All aqueous filtrates and water-alcohol filtrates were concentrated to dryness in vacuo. The residue remaining was found to be diketopiperazine. Thus, during the course of this reaction the authors separated phthalide as an intermediate compound, of peculiar hydrazineamidine structure, and also phthalylhydrazide and diketopiperazine as final products. The separation of these substances confirms the proposed structure (V) and permits an assumption as to its decomposition, as per the following scheme:



To confirm the accuracy of the proposed structure for the above-given compound, the authors arranged the following reactions.

3. Heating of the hydrazide of N,N'-diphthalylglycyldiketopiperazine with absolute alcohol. 0.8 g of the hydrazide of N,N'-diphthalylglycyldiketopperazine, obtained from the preceding experiment, was placed in a flask with a reflux condenser, and 25 ml of absolute alcohol added. Upon heating to boiling for one hour, a precipitate resulted, which was filtered off after cooling and washed with alcohol. The substance isolated was insoluble in either water or alcohol, but was recrystallized from boiling 50% alcohol. M.p. 340°. From its

properties, it appeared to be the phthalylhydrazide. To the alcoholic filtrate with a basic reaction after concentration in vacuo, there was added absolute alcohol. The resulting substance was filtered off, with protection against moisture of the air (through a calcium chloride tube), was washed with absolute alcohol, and dried over P_2O_5. The substance melted at 200° with decomposition in a sealed capillary, and was readily soluble in water, alcohol; poorly so in ether. It gave the anhydride reaction and the ninhydrin reaction, as well as a biuret reaction of the tripeptide type, and represented N,N'-diglycyldiketopiperazine (I).

3.180 mg substance: 0.662 ml N_2 (23°, 743 mm). 3.075 mg substance: 4.770 mg CO_2; 1.660 mg H_2O. 3.020 mg substance: 4.700 mg CO_2; 1.550 mg H_2O. 3.020 mg substance: 4.695 mg CO_2; 1.695 mg H_2O. Found %: N 23.94; C 42.30, 42.40, 42.30; H 5.04, 5.75, 6.20; $C_6H_{10}O_4N_4$. Calculated %: N 24.5; C 42.10; H 5.26.

Analysis of this substance clearly indicated its hygroscopicity.

4. Ionophoresis of N,N'-diphthalylglycyldiketopiperazine hydrazide. 0.5 g of the substance was dissolved in aqueous alcohol and subjected for 48 hours to ionophoresis, the cathode solution being changed after 24 hours. After 24 hours the cathodic solution was basic, the anodic acid. The intermediate portion was neutral. After 48 hours the intermediate portion and the anodic portion were completely neutral. Reactions: in the first 24 hours of ionophoresis: a) positive ninhydrin and anhydride reactions in the cathode solution; b) negative ninhydrin and positive anhydride reactions in the middle portion; c) complete absence of any substance in the anode solution.

Analysis of the cathode solution in the second 24 hours of ionophoresis. The cathode solution was basic. The ninhydrin and anhydride reactions were positive. Under the microscope, a drop of the solution after evaporation showed the presence of diketopiperazine. Upon dilution of the middle portion with water, a precipitate separated, which was filtered off and washed with water. By analysis the substance represented phthalylhydrazide.

5. Elimination of the phthalyl group in N,N'-diphthalylglycyldiketopiperazine [9]. The suspension, containing 2.44 g (0.005 mole) of N,N'-diphthalylglycyldiketopiperazine and 10 ml of 1 molar alcoholic hydrazine hydrate solution in 30 ml of absolute alcohol, was heated under reflux for 1 hour. After cooling to room temperature, the precipitate was filtered off and washed with absolute alcohol.

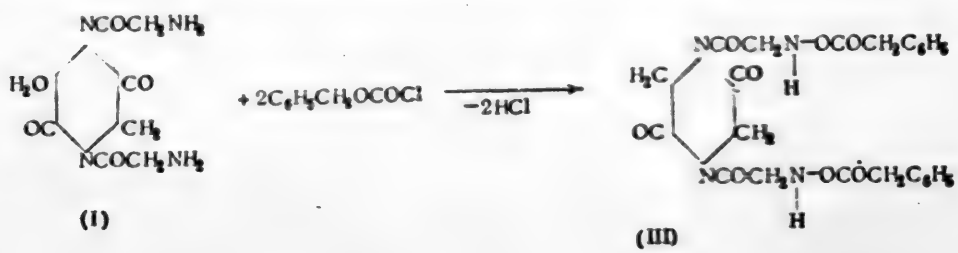
Analysis of the precipitate: did not give the biuret test, but during the course, copper reduction occurred. There should have resulted 1.62 g of phthalylhydrazide from this reaction, by theoretical removal of the phthalyl group, but instead, 2.0 g resulted. The precipitate was therefore treated with 50% alcohol, having placed it on a Buchner funnel. A negligible portion of the precipitate remained insoluble, and from its properties, represented the initial N,N'-diphthalylglycyldiketopiperazine (weight 0.45 g). Upon cooling and concentrating the water-alcohol solution, there was separated in all, 1.25 g of phthalylhydrazide (1.32 g according to theory) which corresponded quantitatively to the removal of the phthalyl group.

Analysis of the alcoholic filtrate. To the filtrate, which gave a basic reaction, absolute ether was added and dry hydrogen chloride passed through to a weak acid reaction. The resulting precipitate was filtered off (with protection from moisture of the air) and was washed with absolute ether. The weight of dried precipitate was 0.8 g, which constituted a 66% yield, calculating on the basis of N,N'-diglycyldiketopiperazine dichloride. It gave the ninhydrin and anhydride reactions, the biuret reaction being of the tripeptide type. It melted above 200°, with decomposition, and represented N,N'-diglycyldiketopiperazine dihydrochloride (II).

Titration according to Sorenson-Gavrilov. 0.0732 g of the substance: 2.4 ml of 0.2 N NaOH (respectively, 4.68 ml of 0.1 N H_2SO_4). Found %: NH_3 8.55. $C_6H_{14}O_4N_4Cl_2$. Calculated %: N 18.6; NH_3 9.3.

Titration according to Willstatter. 0.0467g of the substance: 2.9 ml of 0.1N alcoholic NaOH (respectively, 2.9 ml of 0.1 N H_2SO_4). Found %: NH_3 8.8%. $C_6H_{14}O_4N_4Cl_2$. Calculated %: NH_3 9.3.

6. Interaction of N,N'-diglycyldiketopiperazine (I) with carbobenzoxychloride.



(I) (III)

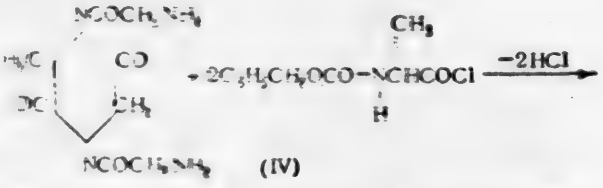
0.3 g of N,N'-diglycyldiketopiperazine was dissolved in 10 ml of water. Simultaneously, 0.41 g (20% excess) of carbobenzoxychloride in ether and 0.1 g of soda in 10 ml of water were added, dropwise, with strong cooling (snow and salt) and with mechanical stirring. The addition lasted for 30 minutes. After completion of the addition and intermixing, stirring was continued for another hour. The aqueous solution was then poured off, and benzene added to the remaining oil. This caused immediate crystallization of the oil, and its transformation to a precipitate which was filtered off and washed with water. The substance was recrystallized from water. The melting point of the dried substance was 110°. Insoluble in water, readily soluble in alcohol and acetone. The ninhydrin reaction was negative, the anhydride reaction positive. Finally a biuret reaction appeared and was of the tripeptide type. From the mother aqueous (neutral) filtrate, the same substance precipitated. Total weight of the substance was 0.4 g, which constituted 81% of theory.

2.365 mg substance: 0.240 ml N_2 (23°, 748 mm). 3.215 mg substance: 0.329 ml N_2 (24°, 742 mm). 3.170 mg substance: 6.735 mg CO_2; 1.440 mg H_2O. 2.415 mg substance: 5.122 mg CO_2; 1.100 mg H_2O. Found %: N 11.51, 11.48. C 57.98, 57.86; H 5.08, 5.09. $C_{24}H_{24}N_4O_8$. Calculated %: N 11.29; C 58.06; H 4.84.

7. Interaction of N,N'-diglycyldiketopiperazine with carbobenzoxyalanylchloride. 0.6 g of N,N'-diglycyldiketopiperazine hydrochloride was dissolved in 10 ml of water and 0.3 g of soda in 10 ml of water was added. Upon strong cooling (snow and salt), and mechanical stirring, 0.56 g of carbobenzoxyalanylchloride in 10 ml of absolute ether was added to the solution, and 0.3 g of soda in 5 ml of water added simultaneously. The addition lasted 30 minutes. After 1 hour of stirring, the ether layer was separated from the aqueous layer in a separatory funnel. The aqueous filtrate was extracted with ether (three times).

Analysis of the water filtrate. The aqueous filtrate was evaporated to dryness in vacuo at 40° on a water bath. Absolute alcohol was added to the residue and once more evaporated to dryness. The precipitate in the flask was transferred to a filter and treated once more with methanol. It was filtered off from the undissolved portion, which was found to be NaCl. Absolute ether was added to the methanol filtrate. The substance which precipitated out was filtered off and washed with absolute ether. The yield was 0.9 g, which constituted 75%, calculating on the basis of the initial hydrochloride salt of N,N'-diglycyldiketopiperazine. The substance melted at 200° with decomposition, and was readily soluble in water; gave a biuret reaction of the tetrapeptide type and a positive anhydride reaction. The ninhydrin reaction was negative. The test for halogen was positive. Repeated reprecipitations from methyl alcohol by ether were of no use. The difficulty in separating the substance from NaCl prompted the authors to repeat the experiment, carrying out the reaction with magnesium oxide instead of soda.

8. Interaction of N,N'-diglycyldiketopiperazine with carbobenzoxyalanylchloride in the presence of magnesium oxide.



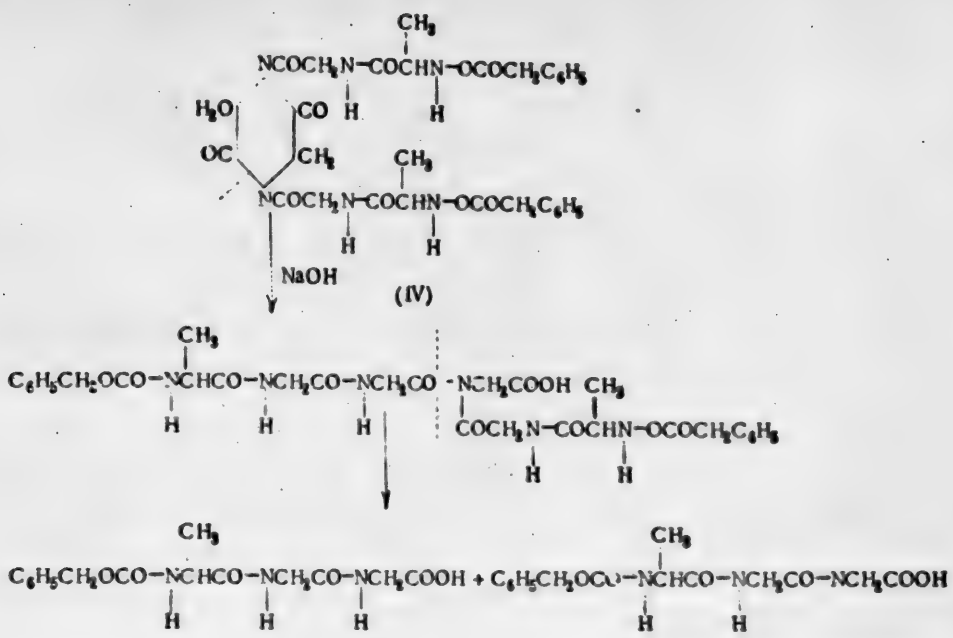
(IV)

The synthesis of carbobenzoxyalanylchloride was carried out according to Bergmann. The resulting chloroanhydride, in the form of an oil, was treated with petroleum ether and then dissolved in absolute ether. 0.8 g of N,N'-diglycyldiketopiperazine was dissolved in 10 ml of water and 0.3 g of MgO added. 1.28 g of carbobenzoxyalanylchloride in absolute ether was added to the solution, with ice cooling and stirring with a mechanical stirrer. The addition lasted 30 minutes, the solution was continuously stirred for another hour. After termination of the reaction (neutral medium), the precipitate was filtered off and the solution evaporated to dryness in vacuo with heat. A very viscous, but transparent oil, was formed. Absolute alcohol was added to it, the resulting precipitate filtered off and washed on the filter with alcohol, a subsequent test for halogen (Beilstein) was positive.

Since $MgCl_2$ is soluble in alcohol and since the resulting substance was insoluble, the total precipitate was left for the night under a layer of absolute alcohol. The precipitate filtered off from the alcohol was treated on the same filter with dry carbon tetrachloride and ether, with absolute ether. The precipitate, dried over H_2SO_4, did not contain halogen. It was readily soluble in water. The anhydride reaction was positive, the ninhydrin negative. The biuret reaction was of the tetrapeptide type. Yield was 1.3 g, which constituted 77%, calculating on the basis of initial hydrochloride salt of N,N'-diglycyldiketopiperazine.

6.760 mg substance: 0.0793 ml N_2 (23°, 742 mm). 2.968 mg substance: 6.110 mg CO_2; 1.303 mg H_2O. 2.976 mg substance: 6.144 mg CO_2; 1.300 mg H_2O. Found %: N 13.21; C 56.37, 56.34; H 5.27, 5.18. $C_{30}H_{34}O_{10}N_6$. Calculated %: N 13.17; C 56.43; H 5.33.

Scheme 5



During attempts to carry out the biuret reaction with 2 N-alkali, asymmetric hydrolysis of this compound was observed on the diketopiperazine ring, and with further decomposition of N,N'-carbobenzoxyhexapeptide to 2-carbobenzoxytripeptide. This cleavage was confirmed by a spectrophotometric curve, indicating an equal mixture of tetra- and tri-peptides. As a result, the authors suggest a decomposition scheme for N,N'-dicarbobenzoxyalanylglycyldiketopiperazine under the action of alkali (vide Scheme 5).

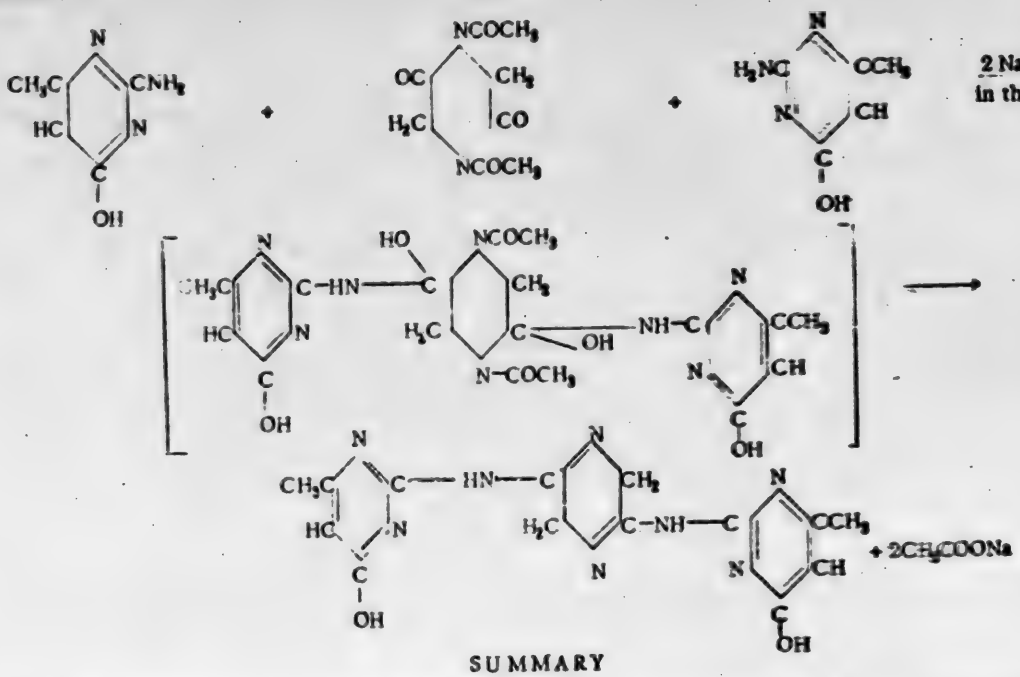
According to the authors' scheme, 2 molecules of protein and 2 diketopiperazines are linked together by 2 tripeptides. The authors have simplified this scheme somewhat, and having utilized the reaction which was discovered between diacetyldiketopiperazine and aminopyrimidines [10] (vide Scheme 6), the authors tried to use the earlier-synthesized N,N'-diglycyldiketopiperazine by combining it with diacetyldiketopiperazine. The reaction proceeded with cleavage of acetic acid, and as the result it was possible to isolate, analyze and characterize the formation of two rings, first the diketopiperazine ring, and second —dihydropyrazine, linked by nitrogens and carbons in positions 2 and 5 to glycine (see Scheme 1, A).

9. Interaction of N,N'-diglycyldiketopiperazine with diacetyldiketopiperazine. Two grams of diacetyldiketopiperazine in 15 ml of alcohol was added to 2.3 g of N,N'-diglycyldiketopiperazine in 20 ml of absolute alcohol. On shaking, everything dissolved. The transparent solution was left standing for 1 hour; a strong odor of the ester, ethyl acetate, was noticed. The medium was basic. Upon passing dry hydrogen chloride into the solution, a precipitate formed, which was filtered off and washed with alcohol. The substance was recrystallized from absolute alcohol. The yield was 3.0 g, which constituted 79% of theory, calculating on the basis of N,N'-diglycyldiketopiperazine taken for reaction. Soluble in water with heating; insoluble in alcohols, gave a positive anhydride reaction, and a biuret reaction of the tripeptide type; ninhydrin reaction was positive upon prolonged heating. M.p. 226°, with decomposition.

1.830 mg substance: 0.346 ml N_2 (23°, 743 mm). 3.211 mg substance: 4.458 mg CO_2; 1.280 mg H_2O. 3.117 mg substance: 4.344 mg CO_2; 1.277 mg H_2O. Found %: N 22.06; C 37.89, 38.03; H 4.13, 4.17. $C_{12}H_{16}N_6O_4Cl_2$. Calculated %: N 22.17; C 38.00; H 4.22.

The compound obtained (see Scheme 1, A) as yet is not the simplified model, No. 2, for the protein structure, but already permits the planning of another method of synthesis of quite a labile structure, which may for a moment exist as a structural fragment of the protein.

Scheme 6



SUMMARY

1. The feasibility of eliminating the phthalyl group in 1,4-diphthalylglycyl-2,5-diketopiperazine by the hydrazine method, with formation of N,N'-diglycyldiketopiperazine, has been demonstrated.

2. An intermediate compound (V) has been isolated.

3. N,N'-Diglycyldiketopiperazine (I), its hydrochloride salt (II), and the carbobenzoxy derivative (III) have been synthesized.

4. The carbobenzoxy derivative of N,N'-diglycylalanine (IV) has been obtained.

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* See Consultants Bureau English translation, page 2219, ff.

** See Consultants Bureau English translation, page 1673 ff.

SPECTROPHOTOMETRY OF BIURET COMPLEXES AS A METHOD OF INVESTIGATION OF PROTEINS AND PEPTIDES

XVI. RELATIVE ACTIVITIES OF COPPER, NICKEL AND COBALT IN THE FORMATION OF THE TRIPEPTIDE BIURET COMPLEX (GLYCYL)

M. I. Plekhan and E. N. Voluiskaya

The biuret complexes of the polypeptides with various metals (copper, nickel and cobalt) represent groups of compounds, each possessing peculiarities. The distinction between one type of complex and the other, and within the range of each group, is displayed with an obvious variability. In a series of copper biuret complexes, the transition from one type of complex to the next is quite evident, but the clearest is found to be the transition from the violet complex of the tripeptide to the red complex of the tetrapeptide (and vice versa [1,2,3]). This transition is marked by a shifting of the absorption maximum, with an increase in absorption intensity in the short wave range, and with a considerable decrease in absorption in the long wave range. For a series of nickel complexes [4], transition from the orange complex of the tripeptide to the canary yellow complex of the tetrapeptide is manifested chiefly by a decrease in the absorption intensity in the range 600-730 millimicrons, which is not so clearly evident at low concentrations. However, the transition from the orange complex of tripeptide to the blue complex of the dipeptide is so clearly evident that it can serve as an indicator for the appearance of dipeptides in the solution.

For the group of cobalt complexes [4], the most intensive application, in a practical sense, is found to be that contrast which gives a reaction of the cobalt complex of the dipeptide, and the absence of reaction with amino acids.

Thus the use of various metals in the biuret reaction has definite advantages, since it permits utilization of the most characteristic peculiarities for each group of complexes. In the first stages of decomposition, as a study of enzymatic, acid and alkaline hydrolysis by the authors has indicated, dipeptides do not appear, but rather formation of chains longer than tripeptides proceeds, with a correlation in changes from violet to red; therefore, in the early stages of decomposition, of greatest interest is perhaps the application of the biuret reaction with copper.

After 1-1,5 hours of acid and of alkaline hydrolysis of gelatin, the appearance of dipeptides was observed, the quantity of which increased within a period of 30 hours. At this stage of decomposition, the use of nickel complexes was found to be especially valuable. In the same cases of hydrolysis, where complete decomposition to the amino acids is required, use of the reaction with cobalt should be an accurate indicator of determination of the reaction.

The question naturally arises whether a simultaneous biuret reaction course with several metals, or a reaction course with one of the metals in the presence of the already-formed complex of another metal, would be possible. A prerequisite condition for this is found to be: a difference in the formation activity of the biuret complex with various metals; a difference in which it would be possible to arrange copper, nickel and cobalt in a given sequence of increasing activity; a sequence in which one metal would be able to displace another (metal) from the complex under any conditions.

The authors have tried to determine experimentally whether such a phenomenon in reality does occur. Experiments on the relative activity of biuret complex formation for the glycyl tripeptide with copper, nickel and cobalt were carried out.

Experiment 1 (Cu + Ni + Co). A solution of the copper biuret complex of glycyl tripeptide was obtained (0.0032 M), the spectrophotometric curve * of which is given in Fig. 1 (Curve I).

* Spectrophotometry was carried out in a König-Martens machine.

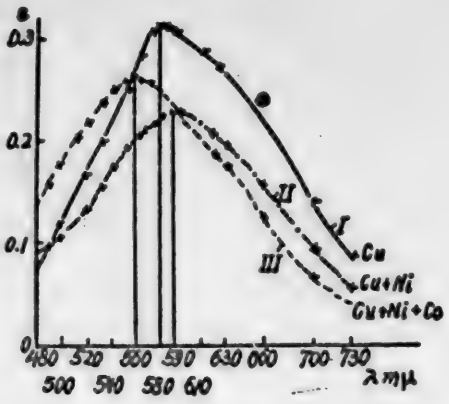

Fig. 1. Spectrophotometric curves for mutual displacement of Cu, Ni and Co in the biuret complexes of the tripeptide (0.0032 M).

3 ml of 0.21 M nickel sulfate was added to 13 ml of a solution of the copper biuret complex. After 1.5 hours, a spectrophotometric curve was taken, II (Fig. 1), (the color of the solution being dark violet). 2 ml of 0.24 M cobalt sulfate solution was then added to 10 ml of the Cu + Ni biuret complex. After 2 hours, Curve III (Fig. 1) was taken. This experiment showed that the appearance of nickel in a solution where the copper complex exists leads to a decrease in the absorption intensity over the entire range of the spectrum from 480 to 730 millimicrons. A very strongly depressed absorption was noted in the wave length range 560-600 millimicrons. The position of the absorption maximum was shifted toward the long waves, and stopped at 590 millimicrons. These changes attest to the fact that nickel partially supplants copper in the complex. A mixture of two complexes is formed —of the copper and nickel complexes. The addition of cobalt to this mixed solution led to a considerable increase of absorption for wave lengths 480-590 millimicrons, i.e., on the very section of the wave length where the cobalt complex possesses the maximum absorption intensity. The position of the maximum was shifted toward the short waves and stopped at wave length 560 millimicrons. Cobalt supplanted one of the metals in the complex. Thus in the solution resulted a mixture of all three complexes. In the sequence of appearance in solution of Cu + Ni + Co, neither nickel nor cobalt were able completely to supplant copper, nor each other.

Experiment 2 (Ni + Co + Cu). A 0.24 M solution of $CoSO_4$ was added to the orange solution of tripeptide biuret complex (Fig. 2, Curve I). After two hours, Curve II (Fig. 2) was taken. A change in the character of absorption occurred, which indicated that cobalt partially supplants nickel in the complex. A mixture of the nickel and cobalt complexes resulted. Cupric hydroxide was added to this mixture and after 1 hour, Curve III was taken, which showed that copper very strongly supplants both nickel and cobalt. Curve III, on the whole, resembles the curve for the copper biuret complex of the tripeptide. Only the existence of a considerably higher absorption in the short wave lengths, instead of the long wave lengths, suggested that any cobalt complex, and also possibly nickel complex, were present in the solution. In the sequence Ni + Co + Cu, the predominant, but not complete, activity belongs to copper.

Experiment 3 (Co + Ni + Cu). The red-brown solution of cobalt biuret complex of the tripeptide (Fig. 3, Curve I) was mixed with nickel hydroxide. Curve II (Fig 3) indicated that nickel displaced cobalt but very little. The addition of copper to this solution, likewise, showed negligible effect. In Fig. 3 (Curve III) it can be seen that absorption in the wave length range 530 to 730 millimicrons increases but little. Copper partially supplants cobalt. But as a whole, the curve preserves its outline inherent for the cobalt complex of the tripeptide. This experiment indicates that in the sequence Co + Ni + Cu, the cobalt complex possesses the greatest stability. Apparently the ability of a metal to form a stable complex is a property to which is not imparted a simultaneous ability to displace another metal from its complex.

In Experiment 1 copper displays an ability to form quite a stable complex, and in Experiment 2 quite a high activity as compared with Ni and Co, but in the 3rd Experiment copper has negligible ability for displacing Co. Nevertheless, on the basis of these experiments it can be concluded that the activity of complex formation and the stability of the complex is lowest for nickel. Although none of the metals display absolute predominant activity of complex formation, none-the-less, they can be arranged in a decreasing order as follows: copper ⟶ cobalt ⟶ nickel. (There is negligible displacement of copper by nickel and cobalt, cobalt is practically unreplaced by nickel or copper, and nickel is completely replaced by copper, but only negligibly so by cobalt).

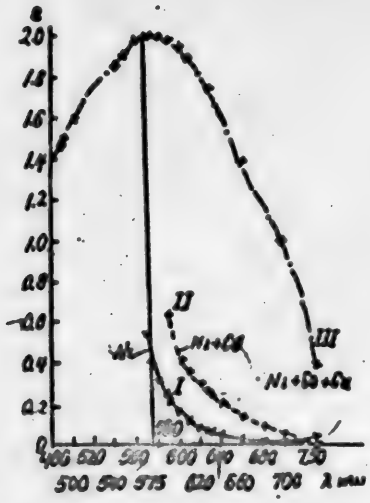

Fig. 2. Spectrophotometric curves for mutual displacement of Ni, Co and Cu in the biuret complexes of the tripeptide (0.032 M).

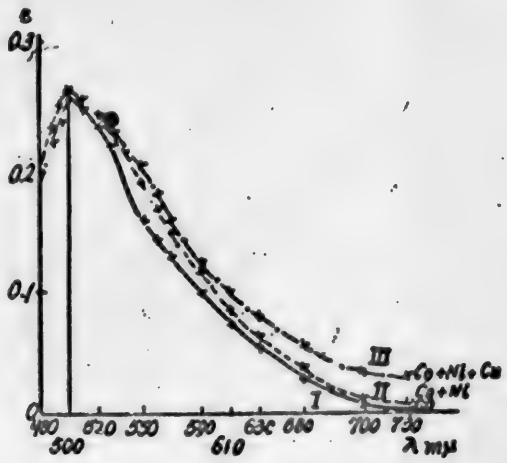

Fig. 3. Spectrophotometric curves of mutual replacement of Co, Ni and Cu in the biuret complex of tripeptide (0.0014 M).

These data do not coincide with the observations of Iesserer [5,6] who analytically studied the stability of Cu, Ni and Co casein complexes, and who found that nickel and cobalt displace copper. Copper itself, in his opinion, was unable to displace either nickel or cobalt.

SUMMARY

The simultaneous introduction of several metals into the biuret reaction complicates the picture of complex formation; therefore, application of the biuret reaction with various metals is best carried out only by separate tests with each metal.

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[3] M. I. Plekhan, J. Gen. Chem., 22, 1495 (1952). **

[4] M. I. Plekhan, A. M. Kan, J. Gen. Chem., 20, 2105 (1950). ***

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* See Consultants Bureau translation, p. 341, 347, 635, 641.

** See Consultants Bureau translation, p. 1675.

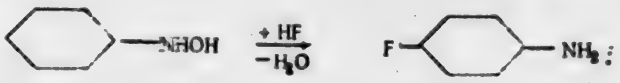
*** See Consultants Bureau translation, p. 2181.

A NEW METHOD FOR THE INTRODUCTION OF FLUORINE INTO THE AROMATIC RING

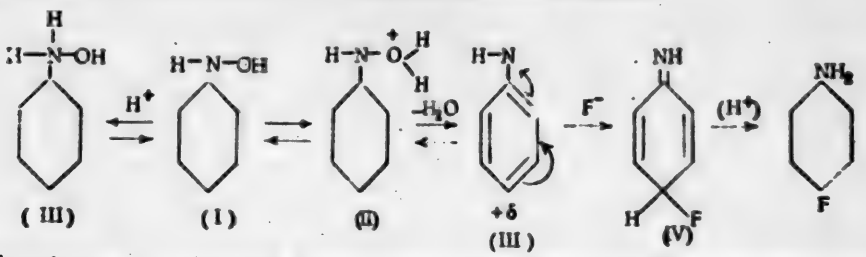
A. I. Titov and A. N. Baryshnikova

The only applicable method for introducing fluorine into the aromatic ring up to the present time has been decomposition of aryldiazonium fluoride or borofluoride [1].

Recently the authors found that the interaction of phenylhydroxylamine with anhydrous hydrogen fluoride produces p-fluoroaniline in good yield:



The mechanism for this discovered reaction may be presented as follows:



Arylhydroxylamine (I) in hydrogen fluoride forms an ammonium cation (II') or oxonium cation (II). The latter, under the influence of strong acid, splits water and converts into the anhydro-cation (III). Due to the presence on the p-carbon of this cation with a +δ charge, it adds the fluoride ion and forms a quinoid product (IV), whose prototropic transformation leads to formation of p-fluoroaniline.

The mechanism so presented very readily explains the various transformations of arylhydroxylamines under the influence of acids when a third component—amine, alcohol, or other substances [2] is involved in the reaction. The data obtained by the authors in their experiments prompted them to adopt an intermolecular character of arylhydroxylamine regrouping, and to reject the generally accepted, up to the present time, interpretation of these reactions as being intramolecular processes [3].

Description of the Experiment

8 g of phenylhydroxylamine, in small portions, was introduced at 0° into 35 ml of anhydrous hydrogen fluoride placed in a copper crucible. After standing for 2 days at +10°, the reaction mass was poured into potash solution and the mixture steam distilled. The distillate fraction was saturated with salt and extracted with ether. After drying the extract and distilling the ether off, 3.8 g of oil remained, which distilled at about 86° under 20 mm pressure, specific gravity of the distillate fraction at 20° was 1.156. These constants corresponded to the literature data for the properties of p-fluoroaniline. Heating 0.3 g of the amine with 0.6 g of acetic anhydride, with subsequent water treatment, gave 0.41 g of the acetyl derivative, melting at 143-145°. A single recrystallization from alcohol gave p-fluoroacetanilide, with m.p. 150.5°, which coincided with the literature data for this product; upon heating its mixed sample with known p-fluoroacetanilide, no m.p. depression was observed.

SUMMARY

A new method for introducing fluorine into the aromatic ring, using the conversion of phenylhydroxylamine to p-fluoroaniline in anhydrous hydrogen fluoride as an example, has been discovered. A reaction mechanism has been given.

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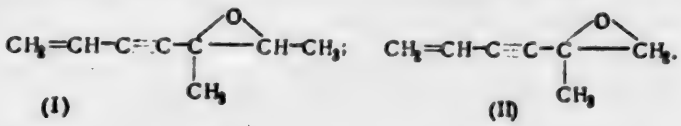
THE INTERACTION OF α-OXIDES OF THE VINYLACETYLENE SERIES WITH OXYGEN-CONTAINING AND WITH ORGANOMAGNESIUM COMPOUNDS. III

F. Ya. Perveev and N. I. Kudryashova

Despite the many investigations in the field of study of olefin oxide interaction with organomagnesium compounds, there has been little study with regard to the position at which the oxide ring is broken as related to structural features of the molecules. To clarify this problem, the authors have investigated interaction of organomagnesium compounds with oxides of the vinylacetylene series. As the objects of investigation, 3-methyloxido-2,3-hepten-6-yne-4 (I) and 2-methyloxido-1,2-hexen-5-yne-3 (II) were selected:



(I) (II)

The vinylacetylene alcohols were synthesized in the usual manner. An ether solution of the oxide was gradually added to an ether solution of the organomagnesium compound with strong cooling (ice and salt) and stirring. During the interaction of ethylmagnesium bromide with 3-methyloxido-2,3-hepten-6-yne-4 (I), an alcohol was isolated in 54% yield – a mobile liquid of pleasant odor, which, in the absence of antioxidants, became viscous upon standing in air, and then transformed into a glassy mass. One of three possible isomeric alcohols might have been expected:

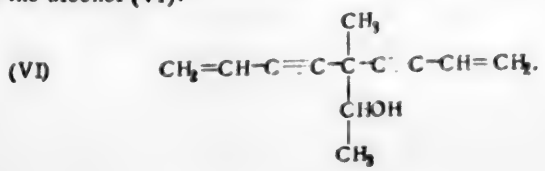
(III) $CH_2=CH-C\equiv C-C(CH_3)(OH)CH(CH_3)C_2H_5$,
(IV) $CH_2=CH-C\equiv C-C(CH_3)(C_2H_5)CHOH-CH_3$,
(V) $CH_2=CH-C\equiv C-CH(CH_3)C(CH_3)(OH)C_2H_5$.

The last alcohol might have formed as a result of preliminary isomerization of the oxide to the ketone under the conditions of the synthesis.

In order to determine the resulting structure, the product was isomerized in the presence of mercury sulfate in methanol solution [1]. After processing of the reaction mixture, the initial product was isolated. It is known [2] that during the isomerization of secondary α-vinylethynylcarbinols, saturated dialkoxyketones result, and upon isomerization of tertiary α-vinylethynyl carbinols, unsaturated monoalkoxyketones predominate.

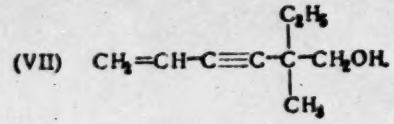
No neutral products were found during oxidation by $KMnO_4$ in the cold, nor after boiling of the acidified solution of obtained substance. This indicated the absence of α-hydroxyacid, which could have formed during oxidation of the alcohol (III). Among the oxidation products, oxalic acid in the form of the Ca-salt of the acid, corresponding to the composition $C_7H_{14}O_3$, was found. On the basis of these data, the authors have assigned the structure (IV) to the product synthesized.

Upon condensing the oxide (I) with vinylacetylenemagnesium bromide, an alcohol was synthesized, consisting of a colorless, mobile liquid, with b.p. 103-104° at 6 mm. The crude product explodes upon heating above 140°. (Distillation was carried out in small lots.) The purified substance was found to be a relatively stable compound. Upon storage in air it becomes yellow after several days. The alcohol remains unchanged, except for negligible resinification, upon treating with 50% H_2SO_4. Upon hydrogenating in alcoholic solution over Raney Ni, a theoretical volume of hydrogen was absorbed (calculating for two double and two triple bonds) with the formation of a saturated alcohol with b.p. 95-96° at 6 mm. The authors were unable fully to determine the structure by ozonization and oxidation; however, the stability with regards to H_2SO_4 indicated the secondary character of the alcohol (VI):



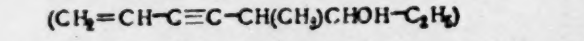
(VI)

Upon interacting ethylmagnesium bromide with 2-methyloxido-1,2-hexen-5-yne-3 (II), an alcohol with b.p. 72-73° at 4 mm was isolated—a colorless mobile liquid. It gradually polymerized upon storage in air. In methanol, with mercury sulfate present, it did not isomerize. The Ca-salt of the acid, composition $C_8H_{12}O_2$, was separated among the oxidation products. Thus, on the basis of the data obtained, the authors gave the structure (VII) to the compound synthesized:



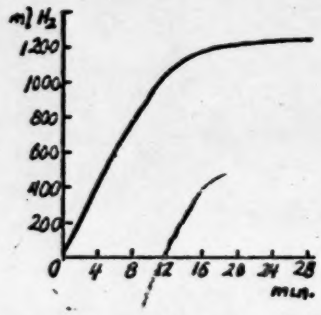
(VII) $CH_2=CH-C\equiv C-C(C_2H_5)(CH_3)-CH_2OH$.

The absence of secondary β-vinylacetylene alcohol also



$(CH_2=CH-C\equiv C-CH(CH_3)CHOH-C_2H_5)$

indicated the fact that the isomerization product of the given oxide does not react with organomagnesium compounds.



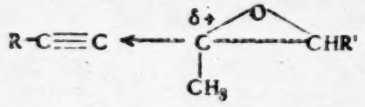
By condensing the oxide (II) with vinylacetylenemagnesium bromide, an alcohol was synthesized—a mobile, gradually-polymerizing liquid. It was not changed by treatment with 50% H_2SO_4. Thermally unstable. Exploded upon heating above 140°. Was fully hydrogenated over Raney nickel in alcoholic solution. The hydrogenation curve is given.

The authors have assumed structure (VIII) for the synthesized alcohol.

(VIII) $CH_2=CH-C\equiv C-C(CH_3)(CH_2OH)-C\equiv C-CH=CH_2$.

Thus it has been established that during interaction of asymmetrically-disubstituted and trisubstituted oxides of the vinylacetylene series with organomagnesium compounds primary and secondary alcohols are respectively formed, i.e., rupture of the oxide ring occurs at that carbon which is directly adjacent to the triple bond, while the olefin oxides of similar structure [3] give, respectively, secondary and tertiary alcohols, i.e., rupture of the oxide ring occurs at the more hydrogenated carbon atom.

This difference in rupture of the oxide ring is explained by the fact that rupture of the oxide ring occurs under the action of organomagnesium compounds at the more positively-charged carbon atom. Just as the triple bond has the ability to attract electrons to itself, in a manner similar to that of the carbonyl groups, so there is always produced at the α-carbon atom of the oxide a more positive charge.



$R-C\equiv C \leftarrow C(\delta+)(O)(CH_3)-CHR'$

EXPERIMENTAL

1. Synthesis of 3-methyl-3-ethyl-hepten-6-yne-4-ol-2 (IV). 30 g of the oxide (I), diluted with a triple volume of absolute ether, was gradually added to an ether solution of ethylmagnesium bromide. The reaction flask was cooled (ice and salt). The yield of alcohol is decreased when cooling is inadequate. After all of the oxide was added, the reaction mixture was left overnight. The organomagnesium complex was then decomposed with a 30% solution of acetic acid. The ether solution was separated, the aqueous—treated twice with ether. The ether extracts were dried with Na_2SO_4. The ether was distilled off and the remaing product redistilled in vacuo. After a triple distillation, 20 g (54%) of the alcohol, with b.p. 81-82° at 10 mm, resulted; d_4^0 0.9216; d_4^{18} 0.9002; n_D^{18} 1.4824; MR_D 48.23; calculated 47.44.

0.0765, 0.0944 g substance: 0.2206, 0.2715 g CO_2; 0.0727, 0.0897 g H_2O. 0.1448, 0.1227 g substance: 24.3, 20.1 ml CH_4 (19°, 766.0 mm). Found %: C 78.68, 78.75; H 10.63, 10.68; active H 0.681, 0.681. $C_{10}H_{16}O$. Calculated %: C 78.89; H 10.59; active H 0.662.

Oxidation of the alcohol (IV). This was carried out in the cold with 3% $KMnO_4$ solution. 9.4 g of the substance was taken and 48.5 g of $KMnO_4$ was used for the oxidation. The MnO_2 was filtered off and washed with hot water. A portion of the solution was distilled off from the filtrate, in which neutral substances were not found. The remaining solution was then evaporated to a small volume, acidified with 10% H_2SO_4, and boiled under reflux. With further treatment, neutral substances and volatile substances were not found. Among the non-volatile substances, oxalic acid, with m.p. 182° was isolated (mixed sample did not give depression) and an hydroxyacid of the composition $C_7H_{14}O_3$, which was isolated as follows: the basic solution, after removal of the volatile acids by distillation, was treated with ether, the ether evaporated and to the remaining oily product, 15 g of calcium carbonate and 50 ml of water added. The mixture was boiled under reflux for 2 hours. The precipitate was filtered off and washed several times with water. The filtrate was evaporated in vacuo. The remaining viscous mass was placed in a vacuum desiccator. The resulting slightly-yellow powder was dried to constant weight at 105-110°, and was calcined.

0.0876 g substance: 0.0140 g CaO. Found %: Ca 11.5. $(C_7H_{13}O_3)_2Ca$. Calculated %: Ca 12.1.

2. Synthesis of 2-methyl-2-ethylhexen-5-yne-3-ol-1 (VII). 17 g of the substance (66.5%), with b.p. 72-73° at 4 mm was obtained from 20 g of the oxide (II): $d_4^{17.5}$ 0.9041; n_D^{19} 1.4889; MR_D 44.1; calculated 42.9.

0.1146, 0.0979 g substance: 0.3323, 0.2798 g CO_2; 0.1063, 0.0901 g H_2O. 0.1487, 0.1369 g substance: 26.02, 23.82 ml CH_4 (18°, 773 mm). Found %: C 78.05, 78.00; H 10.38, 10.30; active H 0.738, 0.734. $C_9H_{14}O$. Calculated %: C 78.21; H 10.21; active H 0.729.

Oxidation of alcohol (VII). This was carried out by the above-indicated procedure. 5.5 g of the substance was taken, and 33 g of $KMnO_4$ was used for the oxidation. No neutral products were found, nor any volatile acid among the oxidation products. An hydroxyacid of composition $C_8H_{12}O_3$ was found.

0.1272 g substance: 0.0230 g CaO. Found %: Ca 12.92. $(C_6H_{11}O_3)_2Ca$. Calculated %: Ca 13.17.

3. Synthesis of alcohol (VI). 40 g of dry vinylacetylene was passed into an ether solution of ethylmagnesium bromide. The reaction mixture was left for the night. Then, with cooling (ice and salt), 34 g of the oxide, diluted with a triple volume of absolute ether, was added dropwise. A strong resinification was observed. After all of the oxide had been added, stirring was continued for another 3 hours. The resulting organomagnesium complex was decomposed with 30% acetic acid solution. The ether layer was separated, and washed with water; the aqueous layer was treated three times with ether. The ether extracts were added to the basic solution and dried over Na_2SO_4. The ether was distilled off, and the remaining product redistilled in vacuo. 20 g of the alcohol, with b.p. 103-104° at 6 mm, was isolated; d_4^0 0.9597; d_4^{11} 0.9399; n_D^{11} 1.5225; MR_D 56.6; calculated 54.2.

0.1461, 0.0930 g substance: 0.4576, 0.2821 g CO_2; 0.1085, 0.0693 g H_2O. 0.0922, 0.1153 g substance: 13.3, 15.9 ml CH_4 (17.5°, 755.8 mm). Found %: C 82.67, 82.71; H 8.30, 8.33; active H 0.596, 0.596. $C_{12}H_{14}O$. Calculated %: C 82.83; H 8.11; active H 0.578.

Hydrogenation of alcohol (VI) was carried out over Raney Ni in absolute alcohol. 10.5 g of the substance was taken. 8.2 liters of hydrogen was used. The calculated volume was 8.1 liters. After completion of the hydrogenation, the catalyst was filtered off and the ethyl alcohol distilled in vacuo. The remaining product redistilled at a temperature of 107-108° at 10 mm. There resulted a colorless liquid with faint odor: d_4^0 0.8609; d_4^{17} 0.8458; n_D^{17} 1.4471; MR_D 58.9; calculated 59.1.

0.0925, 0.1018 g substance: 11.9, 13.0 ml CH_4 (20°, 754 mm). Found %: active H 0.524, 0.520. $C_{12}H_{26}O$. Calculated %: active H 0.541.

4. Synthesis of alcohol (VIII). 40 g of the oxide (I) was taken. 23 g of the substance, with b.p. 109-110° at 8 mm resulted. The alcohol consisted of a colorless liquid which turned yellow on standing. d_4^0 0.9668; d_4^{20} 0.9476; n_D^{20} 1.5292; MR_D 52.09; calculated 49.58.

0.0799, 0.0836 g substance: 0.2410, 0.2526 g CO_2; 0.0553, 0.0563 g H_2O. 0.0830, 0.1136 g substance: 13.3, 17.6 ml CH_4 (21°, 753 mm). Found %: C 82.26, 82.39; H 7.65, 7.53; active H 0.645, 0.627. $C_{11}H_{12}O$. Calculated %: C 82.5; H 7.5; active H 0.630.

Hydrogenation of alcohol (VIII). This was carried out over Raney Ni in absolute alcohol. 3.5 g of substance was taken. 3052 ml of hydrogen was used for the hydrogenation (19°, 767 mm). The calculated volume of hydrogen was 2940 ml. A substance with b.p. 95° to 96° at 7 mm resulted—a colorless liquid with faint odor; d_4^{20} 0.8427; n_D^{20} 1.440; MR_D 53.8; calculated 54.5.

0.0920, 0.0986 g substance: 14.3, 13.9 ml CH_4 (19°, 752 mm). Found %: active H 0.635, 0.575. $C_{11}H_{24}O$. Calculated %: active H 0.586.